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THE MEDICAL CLINICS
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Volume 6 Number 3

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OBSERVATIONS ON THE PROGRESSIVENESS OF DIABETES

RECENT publications from this Institute[1, 2] have dealt with the question of the progressiveness of diabetes. It is certain that function overstrain is by far the most important cause of the familiar downward progress. The question whether it is the only cause, and whether complete freedom from functional overstrain can keep all typical cases from progressing downward, can be answered only by means of a sufficiently large series of cases in which the functional overload has been kept absent or slight. We know that children and young persons are subject to slow but sure aggravation of their diabetes when they are permitted to have hyperglycemia without glycosuria. When hyperglycemia is avoided by successful avoidance of overfeeding and infections we are convinced that downward progress is either prevented or greatly retarded. The occurrence of very slow downward progress under these circumstances might indicate either that there is some progressive factor in diabetes independent of functional overstrain, or that the blood-sugar is not a sufficiently delicate indicator for the complete prevention of such overstrain. Evidently the latter assumption is sometimes correct; for example, a young person in the early mild stage of diabetes will sometimes show normal blood-sugar for a time when placed on a diet very low in carbohydrate and

very high in fat and calories, but hyperglycemia always results later from this functional overload. It may be a question whether the hyperglycemia becomes manifest soon enough to give warning before damage from the functional overload has occurred. The best information on the problem is obtained by collecting as many cases as possible, which have been kept entirely or nearly free from the signs of functional overstrain, and observing whether downward progress has been correspondingly prevented nearly or completely. This was the purpose of the publications already mentioned.

As the duration of such observations is an important feature, my best material for the purpose is found in cases which first came under observation in the Rockefeller Institute, 1914–17. Unfortunately, the great majority of these cases were subjected to reckless overfeeding with fat and total calories. The fact that only some of the milder cases have survived, and all the children and young persons and all the adults with severe diabetes have died under this treatment, stands as a sufficient warning against this method and serves sufficiently as a control of the results obtained under the method of caloric limitation which I have always advocated. The following 4 cases throw some light upon the question of downward progress:

The first case was No. 24 in the Rockefeller Institute series.[3] This man was aged thirty-six years at the known onset of his diabetes, and forty-four years at his admission to the Rockefeller Institute Hospital in November, 1914. In the eight-year interval he had progressed downward from a mild to an extremely severe stage of diabetes. Glycosuria had been present throughout almost the entire time, and glycosuria, acidosis, lipemia, emaciation, and weakness were intense at the time of admission. With a height of 173 cm. (5 feet, 9½ inches) and normal weight of 75 kg. (165 pounds) the weight at admission was 44.2 kg. (97¼ pounds), or 59 per cent. of the original weight. The degree of undernutrition required to control this condition was illustrated by the previously published calculation[4]:

From November 30th to February 2d the following calculation can be made:

	Sixty-five days.	Per day (average).	Per day per kg.*
Protein in diet	1,655.8 gm.	25.40 gm.	5.80 gm.
Total nitrogen in diet	264.9 "	4.07 "	0.09 "
Alcohol calories	23,362.0 "	359.4 "	8.00 "
Food calories	28,294.0 "	434.6 "	10.00 "
Total calories	51,611.0 "	794.0 "	18.00 "

* On 44 kg. weight.

The published record extended to June, 1917. The weight was then 45.5 kg. (100 pounds). The diet had never averaged higher than 70 gm. protein, 10 gm. carbohydrate, and 1500 calories. During his entire time at home the patient had carried on his regular business with only six days' total absence on account of colds.

This same condition continues today. Glycosuria and acidosis remain continuously absent. Slight hyperglycemia has been the rule rather than the exception, but it is permissible in a case of this type because the age involves less tendency to progressiveness than in younger persons and children. Inherent non-progressiveness of the condition cannot be assumed as an explanation of the good result or an excuse for the high mortality among adults with similar or milder cases on excessive diets in this series. We have here a decisive contrast between two periods: first, eight years with active symptoms and extreme downward progress; second, eight years on reduced diet without symptoms and without downward progress. The case is still severe and the tolerance low. It is known that diabetes is hardest to control in the severe stage. What has been accomplished for this patient can be accomplished for all patients of this type, granted fidelity to diet and the absence of any unusual complications. With milder cases the results are correspondingly easier and better. For typical patients of this age or older the question of spontaneous downward progress is definitely decided in the negative.

The second case was No. 66 in the Rockefeller Institute series. This girl was received for treatment in March, 1916,

aged sixteen years, four or five months after the apparent onset of the diabetes. The height was 158 cm. (5 feet, 3½ inches) and the weight 50 kg. (110 pounds). Glycosuria and other symptoms were quickly and easily controlled. By undernutrition the weight was reduced to 45 kg. The maximum prescribed diet averaged 80 gm. protein, 45 gm. carbohydrate, and 1500 calories. Violations of diet at home took the form of stealing fat, particularly butter, because this was hardest to detect in examinations. Increases of weight as high as 55.4 kg. and returns of symptoms were the result. The published record extended to October, 1917, when the weight was 51.7 kg. and the diet had been reduced to 70 gm. protein, 60 gm. carbohydrate, and 1275 calories.

Occasional trangressions of diet with fat resulted in further loss of tolerance, requiring reduction of diet and weight to keep the blood-sugar normal. A state was reached in which the tolerance was as low as 50 gm. protein, 5 gm. carbohydrate, and 1000 calories, and the weight fell to about 36 kg. (85 pounds). Therefore, during the past three years the patient has been kept almost continuously under the care of a trained nurse at her home. The tolerance and weight have thus been kept stationary except for the slight influence of a few violations of diet. At the age of twenty-one years the patient remains in a state of moderately severe diabetes, capable of light physical and mental activity, but without appreciable downward tendency.

A comparison was previously drawn[6] between this patient and a boy of similar age, who was subjected to overfeeding to the extent of 50 calories per kilogram of body weight, the attempt being made to build up weight especially with a high ration of fat, while merely glycosuria was avoided and hyperglycemia was disregarded. This boy died within two years from the onset of his diabetes after typical downward progress. In addition to these contrasting results in these 2 similar cases we now have the comparison between two periods in the girl's history: first, a period of three years in which both the weight and the blood-sugar were frequently elevated by surreptitious additions of fat to the diet, with accompanying downward progress of marked

degree; second, a period of three years in which violations of diet have been few and in which downward progress has likewise been barely perceptible. The susceptibility of this patient to typical downward progress is thus demonstrated, but the existence of any cause other than functional overstrain has not been apparent in six and a half years of observation.

The third case was No. 76 in the Rockefeller Institute series.[7] When first seen in March, 1917, this boy was aged four years, was 106.6 cm. (3 feet, 6⅞ inches) in height and weighed 15 kg. (33 pounds). Diabetes had come on apparently in association with a slight middle-ear infection, and the good fortune of obtaining the case for treatment within about three weeks after the apparent onset permitted the quickest and most favorable result. Only slight undernutrition was required, the weight being reduced to 14.4 kg. The published record extended to October, 1917 and the following note was made: "The prescribed diet was 55 gm. protein, 80 gm. carbohydrate, and 980 calories, representing 3.8 gm. protein and 68 calories per kilogram diminished by weekly fast-days to about 3.3 gm. protein and 58 calories average. This diet is permitted with the idea of permitting the boy to grow if possible. A close watch is being kept, and any appearance of slight hyperglycemia will be the signal for a reduction of diet. The carbohydrate has since been increased to 100 gm. and the child is growing steadily, the blood-sugar remaining normal. The case was received at a favorably early stage, and the treatment has been followed with the utmost fidelity. The result in this four-year-old patient is favorable to date."

This boy has remained constantly faithful to diet while attending school and carrying on all activities normal for his age. Spontaneous downward progress has never been apparent. On the other hand, the following list of infections and accidents have been encountered:

October, 1917, fever and diarrhea of unknown origin, lasting one week.

March, 1918, a similar attack.

September, 1918, "intestinal toxemia" again.

December, 1918, severe influenza with bilateral otitis media, requiring puncture of both drums. Death was narrowly escaped.

April, 1919, "intestinal toxemia."

June, 1919, arm broken at play and set under ether anesthesia.

November, 1919, measles.

January, 1920, influenza with high fever; condition serious.

October, 1920, milder influenza complicated with bronchitis.

January, 1921, scarlet fever with enlarged cervical glands, the entire duration of illness being over a month.

The attacks of influenza, measles, and scarlet fever apparently did not indicate a subnormal resistance, for the patient's parents and 3 brothers are healthy and robust and some or all of them suffered from the same infections at the same times. Especially one of the influenzal infections was of the virulent form which was epidemic during the war, and the patient seemed to show excellent resistance in overcoming it.

The attacks of "intestinal toxemia," of unknown nature, were always attended by a marked temporary lowering of food tolerance. We have records of 2 other diabetic children who have been subject to such attacks and whose tolerance has been similarly reduced. Whatever the nature of the infection, there has been a strong suspicion that it involved pancreatitis, though the only evidence for this assumption consists in the striking transitory impairment of assimilation.

This patient was not observed by us during any of the above infections, but was treated by his family physician and by his father, who had become a skilled dietitian. The latter followed the plan of reducing the diet sharply, especially in fat, with the onset of every infection. Accordingly, no more than brief traces of glycosuria and acetonuria appeared at any time. This is believed to be the reason why the long series of infections showed scarcely any lasting effect upon the food tolerance. The function of the islands of Langerhans is undoubtedly impaired by infection and intoxication, but this impairment is manifested by the usual diabetic symptoms. When these symptoms are controlled by suitable reduction of diet lasting injury of the islands is prevented as far as possible. On the other hand,

there is evidence that the island cells, when damaged by infection or intoxication, are highly susceptible to functional overstrain. It is probable that more damage usually results from the functional overstrain indicated by glycosuria during an infection than directly from the infection itself.

Notwithstanding the handicaps described, this boy gained gradually in assimilation, so that diets as high as 1100 calories were tolerated with consistently normal plasma sugar both fasting and during digestion. His photograph was published in my article on diabetes in Nelson's Loose Leaf System of Medicine in 1920, as an illustration of a good clinical result after three years of diabetes, at this early age.

In 1922 there was another attack of mild influenza and subsequently a severe one of "intestinal toxemia." The latter seemed to damage the tolerance, for though glycosuria was controlled, hyperglycemia persisted on reduced diet. The patient, therefore, entered the Physiatric Institute in October, 1922. This was his only entrance to a hospital since leaving the Rockefeller Institute in 1917.

His height today is 135 cm. (4 feet, 6 inches) and his weight is 21.4 kg. (47 pounds). His growth has not kept pace with that of his brothers, one of whom is 6 feet tall. The father is rather short in stature, and the possibilities open are that this boy more closely resembles his father, or that he has been stunted by his numerous infections or by his diabetes and attendant limitation of diet. The last factor should not be excessively emphasized, since low diet usually does not seriously limit growth in length in children and young animals unless there is also marked emaciation, which has been lacking in this case. On the other hand, we must face the fact that limitation of diet will hinder the growth of children to some extent, and that the best results from the diabetic standpoint may involve a state which is inferior to that of the strictly normal child.

This boy's blood-sugar came to normal with three days of low diet in the Institute, and it seemed probable that his tolerance could be brought up to something near the former level. Instead of such a program, he has been placed on the treatment

with Dr. Banting's pancreatic extract. This introduces a new hope of building up weight and strength. For the present purpose the important fact is that this boy was four years old when first seen with diabetes, and he still looks and feels well at the age of nine years. With unusual care in diet, his tolerance has risen rather than fallen during five years, even against a serious handicap of infections, and he has at the same time lived a happy, normal life. The avoidance both of emaciation and of the invalid state of mind was made possible by the early stage at which treatment was begun and by continuous fidelity to it. If there has been a fall of tolerance due to infection in recent months, the only wonder is that it has been so slight. No inherently progressive tendency has been manifest, and the result stands as a challenge to the radically different results ordinarily obtained with less careful dietary restriction.

The fourth case was one of those not published in the Rockefeller Institute series because of the mild character and short duration at that time. The patient was a healthy appearing seventeen-year-old girl, who was found to have glycosuria in a routine examination on entering Vassar College early in October, 1917. Within two weeks thereafter she was admitted to the Rockefeller Institute Hospital, and the condition was quickly and easily brought under control. The details of the initial treatment are not available at this moment, but only slight undernutrition was required, and since then only the slight tendency to obesity has been held in check. With a height of approximately 5 feet, 8 inches, the patient has continued to weigh approximately 140 pounds. The diet was weighed for about a year, but since then has been mostly unweighed. The patient has learned to estimate foods with fair accuracy and the treatment has been guided by two standards: first the body weight, and second the blood-sugar. She is now twenty-two years old, has graduated from Vassar College, and is studying in Europe. The plan of treatment employed has been more lax than would be compatible with safety in the vast majority of cases at this age. The condition appears to be unusually mild, and the point of interest is to see whether downward progress

will occur if only obesity and hyperglycemia are avoided. A control observation is also afforded, because when this patient's glycosuria was discovered urinalyses were made on all members of the family, and glycosuria was discovered in a brother of nearly the same age. The brother has been careless in diet, and by reason of the mildness of his disease has been able to ignore the existence of glycosuria for a long time. He is now suffering from loss of weight and severe neuritis, and it is evident that his diabetes is reaching a severe stage.*

Two lessons may be drawn from this case: First, the physical examination of students, which is becoming customary in most educational institutions, should invariably include a urinalysis. Many mild cases of diabetes will thus be discovered months or years earlier than they would be revealed by clinical symptoms, and more favorable results will thus be possible from treatment. Second, even the mildest cases are susceptible to aggravation from functional overstrain, and no valid distinction has ever been drawn between true diabetes and any chronic form of glycosuria accompanied by hyperglycemia. It is important not to be too optimistic concerning non-progressiveness in mild cases, or to be too pessimistic concerning an alleged inevitable progressiveness of severe cases.

Few cases in ordinary medical practice are suited to furnish information concerning progressiveness of diabetes on a basis of scientific accuracy, comparable to the observations on diabetic dogs which are kept shut up in cages. Mere decline of tolerance in patients supposedly following a diet at home is practically worthless as evidence, because those who seem most trustworthy sometimes become proficient in violations of diet which are hard to detect, as illustrated in the second case described above, and the most careful watching by family or nurse can be circumvented by sufficient effort. Proper treatment and study of a large series of cases under exceptionally accurate

* Case No. 28 in the Rockefeller Institute series[3] is another example of juvenile diabetes of unusually mild and non-progressive type, which under careless treatment with high diets reached a severe stage within three years and then ran a rapidly fatal course.

control would have been the best means for settling this important question before it became confused by the new element introduced by the treatment with pancreatic extract, and for this reason the loss of this opportunity at the Rockefeller Institute was particularly unfortunate.

The existing information shows a very strong contrast between cases thoroughly treated with restricted diets for the relief of functional overstrain, and those treated with high diets in the fallacious attempt to "build up" the patient. Clinical and pathologic studies seem to agree in their failure to reveal any cause of progressiveness of diabetes outside of infections and functional overload. In the large series of cases in the Physiatric Institute any downward progress has been routinely assumed to be due to one of these two causes rather than to any mysterious and inevitable element, and in the absence of infection a transfer from home conditions to the accurate environment of an institution has invariably seemed to halt such progressiveness. Whether or not the question is considered settled from the standpoint of scientific theory, we have no doubt that the best practical results are obtained by treatment on this assumption.

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TREATMENT OF ARTERIAL HYPERTENSION

THE records of 3 cases here shown will illustrate our methods and results in the treatment of arterial hypertension. The theoretic aspects of the subject, the relation to nephritis, and other doubtful matters can best be considered in a more complete publication elsewhere.[1] We shall be content here with a brief statement of clinical facts.

Patient No. 1 (Case No. 188): This patient is an Episcopalian clergyman, married, and aged thirty-five years at the time when he was first referred to this Institute by Dr. Russell J. Verbrycke, of Washington, D. C., March 15, 1920. The family history was unimportant. The chief feature in the patient's earlier history was that at the age of twelve he developed osteomyelitis at the junction of the middle and lower thirds of the right femur. Notwithstanding several operations a discharging sinus persisted. While in college he was troubled with cardiac palpitation and pounding in his head. Later in theological seminary he had apparently an acute exacerbation of a chronic nephritis, and suffered more from the above symptoms, together with headaches, dizziness, and epistaxis. He was placed on a Karell diet for about six weeks, then came to Washington in 1913, and led an active life without medical attention, but with more or less symptoms for three years. In 1916 the systolic blood-pressure was found to be 218 mm. Medication was prescribed, but no dietary restrictions. He spent the summer of 1919 in Newfoundland and had much distress from palpitation, pain, and gripping sensations in the heart region. Since then he has had severe attacks of angina pectoris. He had had an attack of ulcerative keratitis about once each year, but has retained good vision. Several abscessed teeth have been removed and the others pronounced healthy. There has been no polyuria or nocturia. The blood-pressure has remained constantly between 200 and 236 mm. and the condition at admission was considered serious.

Physical Examination.—Height 5 feet, 6½ inches, weight 130 pounds. Body thin rather than fat. The patient is over-nervous and excitable in type and drives himself to the utmost, physically and mentally. The general examination is negative except for a moderately enlarged heart with a systolic murmur at the apex and accented aortic second sound; action markedly violent on slight exertion; superficial arteries palpably thickened. There are several healed scars of incisions and two small discharging sinuses in the lower part of the right thigh. Blood-pressure 214 systolic and 130 diastolic.

Special Examination.—Ophthalmoscopy showed retinal arteries somewhat thickened and tortuous, disks slightly blurred, some scarring, but no active exudate or hemorrhage. Radioscopy showed enlargement and osteoporosis of the femur at the site of the old osteomyelitis and a superficial lamina of bone probably dead, but not yet well separated from the living portion.

Laboratory.—Urine pale, specific gravity 1.008, slight albumin, numerous hyaline and granular casts present, sugar and acetone absent. Phenolsulphonephthalein elimination (reported by Dr. Verbrycke) 60 per cent. in two hours. Blood Wassermann negative; hemoglobin, 104; red cells, 5,992,000; urea, 28; plasma chlorids, 620; plasma sugar 109 mg. per 100 c.c. A glucose tolerance test showed no impairment of assimilation.

Treatment.—No medicines or other artificial measures were employed. The patient was allowed to walk and otherwise exert himself at will. The diet was unrestricted except for careful exclusion of sodium chlorid. Abundant protein and calories were thus taken and no weight was lost, as the prevalent idea that a salt-free diet cannot be made appetizing is entirely imaginary. Gradual improvement followed. By March 21st the pressure had fallen to 170 systolic, 110 diastolic, and by March 26th to 161 systolic, 100 diastolic. Subjective symptoms, though markedly diminished, were still present. Complaints were chiefly of headache and occasional palpitation or angina. The patient remained decidedly nervous and restless.

March 27th experimental administration of 10 gm. sodium chlorid produced little immediate effect. By the following

morning the pressure had risen to 192 systolic, 120 diastolic, and all symptoms were aggravated. Excretion of the salt was very slow, and the urinary chlorid did not fall below 1 gm. in twenty-four hours until April 5th. The symptoms were most violent on April 2d, when the pressure was 206/128, and the patient was in a serious and distressing attack of angina throughout most of the day. Nitroglycerin in full doses reduced the pressure as low as 184/116, but it soon returned to 216/124, with a pulse-rate of 90 to 96 per minute. When the chlorids of plasma and urine had resumed a low level following April 4th, symptoms were again relieved. In a single instance on April 10th the pressure was 192/132. Otherwise the systolic pressure was never above 180, averaged 160 to 170, and on several occasions was 146 to 152. The diastolic pressure remained at 100 to 110.

Though the patient felt greatly improved and serious attacks remained absent, minor attacks of palpitation, angina, and discomfort in the head continued to be rather frequent. By April 24th the pressure had gradually fallen as low as 130 systolic, 72 diastolic, but was liable to rise from slight causes, and the result was by no means perfect. The patient was discharged April 24th, to resume his regular duties at home.

The degree of improvement attained encouraged the patient and his physician to continue the careful salt-free diet at home. Occasional samples of twenty-four-hour urine collections were mailed for analytic control, and the daily sodium chlorid excretion was found usually about 1 gm. The systolic blood-pressure ranged usually between 160 and 180. The patient carried on his full activities, though subject to slight attacks of the kind described. At intervals of several months he was still subject to more serious attacks, in which the blood-pressure rose to 200 or over.

A slow improvement continued, in that the blood-pressure on the whole fell gradually, and symptoms of all kinds became less frequent and less severe. Recently (October 14, 1922) the patient has returned to the Institute merely to spend a vacation while having his general condition checked up. All subjective

symptoms are now regularly absent. The highest pressure observed during this time was 150 systolic and 104 diastolic. The lowest systolic pressure has been 120, the lowest diastolic 78. With the single exception mentioned the pressure taken under various conditions of rest and exertion at various times of day has never been above 140 systolic and 90 diastolic. The urine does not contain albumin or casts. Its chlorid content ranges between 0.9 and 3.9 gm. per day, indicating that the patient has acquired a slight tolerance for salt. The highest plasma chlorid has been 589 mg., the lowest 568 mg. per 100 c.c. Normal concentrations of blood urea (24–29 mg. per 100 c.c.) plasma sugar (105–111 mg. per 100 c.c.) continue. The body weight is 131 pounds. The patient is less nervous than before, feels entirely well, and states that he has been carrying particularly heavy work involving late hours and much fatigue. The discharge from the right femur is still present, but gives no trouble. This result is an unusually successful one in a case of such difficulty.

Patient No. 2 (Case No. 1268): This patient, male, aged fifty, married, graduated as a physician, but for the past twenty years has been a paper manufacturer. The family history is unimportant except that several relatives have died of apoplexy. The personal history was negative except for an appendicitis operation and a suspicion of gall-stones years ago. The patient has been entirely well except for constipation. There is a record of edema of both ankles as long as five years ago. Subjective symptoms began with headache and "rheumatic" pains in elbows, shoulders, and knees two years ago.

At that time albuminuria was present and the systolic blood-pressure is said to have ranged between 140 and 160 mm. There has never been glycosuria. Palpitation has gradually developed and the patient cannot stand physical exertion or lie on his left side on account of it. Complaint is also made of shortness of breath, nocturia, and difficulty in thinking clearly. No relief has been obtained from the pulling of four teeth, changing of glasses, or reduction of smoking from 60 to 15 cigarettes per day. The patient leads an easy, sedentary life, but is con-

siderably worried about his health. He came for examination November 5, 1922, and was admitted for treatment November 9th.

Physical Examination.—Height 5 feet, 11¾ inches. For the past twenty years the weight has been constant at 215 pounds. General examination negative except for slight cardiac enlargement.

Blood-pressure 195 systolic, 100 diastolic, and a soft systolic murmur at the apex.

Laboratory.—Urine free from albumin, casts, and sugar. Blood Wassermann negative. Blood urea 18, plasma chlorids 614, plasma sugar 123 mg. per 100 c.c. A test with 100 gm. glucose caused no glycosuria, but impaired utilization was indicated by the plasma sugar, which at the first hour was 250 mg. and at the second hour 300 mg. per 100 c.c.

Treatment.—The diet was salt free and was limited to 70 gm. protein, 30 gm. carbohydrate, and 700 calories for the purpose of reducing weight. By the time of discharge on November 16th the blood-pressure had fallen to 150 systolic, 80 diastolic. All subjective symptoms were completely relieved except for slight occasional headaches, apparently due in part to constipation. The body weight had fallen to 205 pounds, partly through loss of an invisible edema. The result within the short period of treatment was incomplete, but the patient was instructed as usual in management of his diet at home, and further improvement is expected with fidelity. A patient of this type will generally require the addition of 1 or 2 grams of salt to the diet in order to prevent symptoms of chlorid privation. As no such symptoms had appeared, and as this amount of salt is likely to be obtained accidentally by the average patient, advice concerning any possible addition of salt was deferred until subsequent reports of progress should be received.

Patient No. 3 (Case No. 1259): This patient is a retired business man, married, aged sixty-four years, admitted to the Institute October 24, 1921. His father died of apoplexy at eighty-six years, his mother of paralysis at sixty-four, and one brother of diabetes at fifty-seven. He has 2 sisters living and

well. His personal history is clear except for minor childhood disease. He has used alcohol and tobacco moderately for the past twenty years and has comitted no excesses in work or diet. With a height of 5 feet, 9 inches his weight averaged 165 pounds and at admission was 158 pounds.

Three years ago he had a sudden hemorrhage from the nose, and more or less bleeding occurred during the next three or four months. His systolic blood-pressure was found to be over 200 mm., and he is supposed to have had cerebral hemorrhage without the ordinary symptoms of apoplexy. In May, 1922 there was another such attack, and he discontinued attempts at business. His systolic pressure then was 240 mm. He has never had edema, retinitis, dyspnea, paralysis, or headache, but his memory and mental power have deteriorated and he tires easily on mental or physical exertion. Prior to his admission the patient had received electric treatments, also colonic irrigations, which according to reports had reduced his blood-pressure temporarily as low as 180 systolic, 120 diastolic.

Laboratory.—Urine, specific gravity 1.017, albumin 0.10 to 0.15 gm. per liter, very few hyaline casts, no sugar or acetone. Phenolsulphonephthalein excretion 52 per cent. in one hour. Blood: Wassermann negative, urea 24 mg., plasma chlorid 595 mg., plasma sugar 104 mg. per 100 c.c.

Treatment.—An unweighed salt-free diet was given, which the patient ate well as usual. The decline of weight from 158 pounds on admission to 152 pounds at discharge was probably due to loss of water, though no edema had been visible. The blood-pressure by October 28th had fallen to 200 systolic, 120 diastolic. It remained essentially at this level up to the time of discharge. On occasions the systolic reading was as low as 180 and the diastolic as low as 100, but in a few other instances the systolic was as high as 208 and the diastolic as high as 140. The subjective condition was slightly improved, in that the patient was more cheerful and capable of somewhat greater activity. No symptoms of salt privation appeared on a diet which reduced the sodium chlorid in the urine to 0.2 to 0.5 gm. per day. The patient was discharged November 14th, with a

plain statement that the result was unsatisfactory to date, but the salt-free diet should be continued in the hope of slow improvement.

The case may fall into one of two classes. On the one hand, it is possible that the condition may improve with months or years of strict diet, as observed in the first case described above and in several other cases in our experience. On the other hand, this case may belong to the refractory group, in which organic changes are probably too far advanced to permit of successful treatment by functional relief. The effort at prolonged dietary control is worth while because it is harmless, not a hardship when proper instruction in selection and preparation of food is given, and there is a chance of some degree of benefit even in cases which appear most hopeless at the outset. If the pressure is actually uncontrollable by diet, the prognosis is bad. Patients of the refractory group generally die within a year from some of the well-known accidents of hypertension.

With an experience now of over 200 cases we are able to reaffirm every statement made in an earlier communication.[2] The great majority of cases of hypertension, whether simple or complicated with other conditions, are more or less completely relieved by the single measure of salt-free diet, carried out thoroughly and accurately for a sufficient length of time. The results are not due to chance, psychic influence, rest, reduction of weight, or other imagined agencies. It is a scientific fact that a relation exists between chlorids and vascular hypertension.

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RENAL FUNCTIONAL TESTS AND THEIR VALUE IN UROLOGIC MEDICINE AND SURGERY

Full Description and Discussion of the Various Tests to Be Applied to All Symptoms of Renal Disease.

PERHAPS no methods of combined clinical and laboratory investigation have become more attractive to both internist and surgeon of late years than those that are intended to throw light on renal function. Great as has been the progress in our knowledge of estimates of renal activity, much confusion and doubt as to the value, application, and interpretation of the many proposed tests still exist among practitioners as well as specialists. On the one hand, there is that state of mind which (with the wish father to the thought) desires to find in one procedure an answer to all queries; and, *per contra*, another view of skepticism that goes to the extreme of rejecting and doubting all that is offered; and simply because of the complexity both of the tests and the diversity of opinion as to their respective values.

The matter is not as involved as it may seem. If we remember that the kidney is an organ with a number of functions, that it eliminates water, salt, certain nitrogenous substances and urea, as well as possessing a capacity to reject special bodies or substances of exogenous source (dyes, toxins, etc.); if we remember, too, that the renal activities at any given moment cannot represent the average capacity or the power of accommodation of any one or all of its functions, and that the intake of water and foods must needs have some influence; and, further, if we take into consideration the importance

of all the many other factors (circulatory, neurogenic, inhibitive, etc.) that modify the renal work, then, and then only, will we be prepared to view dispassionately and judiciously the data obtainable through the many important tests that have been proposed.

Space will not permit of a comprehensive review of renal physiology under normal and pathologic conditions, nor to describe in detail the many excellent procedures for investigation of renal function. But, for our purpose, I may be permitted to take up my theme in a sufficiently broad way so that even those working in other fields may be prepared to follow. Therefore, let us divide our subject matter as follows, discussing:

First: The more important methods of investigating renal function, with notes on their significance in non-surgical cases; and

Second: The application and interpretation of these tests in surgical diseases of the urinary tract.

Numerous tests of the renal work have been advised, many of which have never passed the experimental stage. Some were designed with a view to estimating total renal capacity, while others were regarded as furnishing an index of special or single renal functions.

We must remember that a quantitative study of substances excreted in the urine alone is only of value in so far as the figures are related to a measure of the intake of the same substances. To obviate the necessity for such comparative study other procedures have been suggested. Among these we may cite the synchronous estimation of certain substances in the blood and in the urine, and a comparison between the quantities in the blood and the amount of the same substances excreted in the urine during stated periods. As applied to urea, a new and valuable method of this type was devised by Ambard, whose procedure will be discussed later on.

Concerning tests of the performance of special functions we may briefly allude to the sodium chlorid excretion, the nitrogen excretion, and the urea excretion.

Sodium Chlorid Excretion.—The ability of the kidneys to eliminate salts is studied by a comparison of the intake during twenty-four hours, and the output during the same period. A healthy person is said to excrete all but 1 or 2 gm. of the amount of salts ingested. The patient is put upon a fixed diet with a known but not excessive amount of sodium chlorid, and the amount in the twenty-four-hour specimen is estimated. If the study be carried out for several days, a reliable appraisal of the excretion of sodium chlorid by the kidneys can be made. The renal tolerance can be further investigated by adding known amounts of salt in addition to what is in the diet at one dose, with a view to determining the rapidity of its excretion. Normally a kidney should excrete most of the extra sodium chlorid within forty-eight hours, while when salt elimination is interfered with, no increase in the output of salt is observed after this test.

Nitrogen Excretion.—A normal individual excretes an amount of total non-protein nitrogen in the urine that is about 1 to 3 gm. less than that in the food. The renal capacity in regard to nitrogen may be studied, therefore, when the amount of nitrogen in the daily diet and the total non-protein nitrogen excreted in the twenty-four-hour specimen of urine is compared over a period of several days.

Furthermore, the renal tolerance in regard to nitrogen may be studied, according to Monakow, by giving 20 gm. of urea at a single dose, noting how soon the nitrogen of this urea, which amounts to about 10 gm., is excreted in the urine. The greater part of this nitrogen should appear from twenty-four to forty-eight hours normally, while in renal disease only a little of it will be secreted in the urine within the forty-eight hours.

The French authors make a clinical classification of nephritis according to the capacity of the kidney to take care of salts or of nitrogen.

Urea Excretion.—The urea test devised by Ambard concerns the capacity of the kidney to excrete one of the fractions of non-protein nitrogen, namely, urea. Although this test is

one of special functions, it has been regarded as a fair expression of the total renal function.

For a better understanding of the laws of Ambard and the rationale of his procedure let us briefly survey some of the fundamental and pertinent facts of renal physiology. It is well to define and understand both the factors entering into the Ambard quotient, as well as the response of the kidney toward the passage through it of various substances.

By total output of a substance we understand the quantity in weight eliminated in a given time. If the kidneys secrete 1 gm. of urea an hour we speak of the hourly output as being 1 gm. However, the total output is obtained by multiplying the volume of urine expressed in liters or ounces by the concentration. Thus, for example, if the volume is 150 c.c. and the concentration 10 per cent., the total output would be 1½ gm. It is well to take the accepted unit of twenty-four hours for the calculation. If the output obtained for one hour is 2 gm., we calculate the output for the day as 48 gm. (twice 24). It is useful as a measure of comparison to choose such a unit, although this given unit has no actual importance.

Excretion of Substances With and Without a Threshold.—The output of a certain substance by the kidney has been regarded in a certain measure as dependent upon the percentage of the substance in the blood, but this cannot be accepted as always applying. Although this obtains in the case of urea, it is quite different with sodium chlorid and glucose.

As regards urea, the kidneys secrete it so long as the blood contains this substance, and proportionately to the amount contained therein. Thus, in the case of chlorids and glucose, the kidney does not commence to secrete until the percentage of these substances in the blood attains a certain concentration. Below this concentration the kidneys do not allow it to pass. The threshold of excretion, therefore, is the percentage of a substance contained in the blood, above which secretion of that substance commences, and below which it ceases.

According to the present views the substances found in the urine may be divided into two varieties: first, the substances

without a threshold, which are useless to the cellular life and consequently are excremental, namely, urea, ammonia, uric acid, and the various dyes; and second, the substances *with* a threshold, which are useful to cellular life, namely, sodium chlorid, the various salts, glucose, water, etc.

A study of the output of the substances without threshold leads to the development of the so-called procedure of Ambard (the urea coefficient), a method of considerable value in function diagnosis.

Concerning the Excretion of Substances Without Threshold.—In a comparison of the urea content of the blood and the nitrogen content of the food Widal showed that the kidneys offer a certain degree of resistance to the passage of urea, the blood being surcharged with a certain quantity of this substance; that by an automatic adaptation, a state of urea pressure, as it were, is developed in the blood, the percentage varying according to the degree of renal lesion and the amount of albumin ingested. For the same amount of albuminous substance taken in, the degree of urea retention in the blood seems to be about the same, but it varies with the permeability of the kidneys.

Other studies have shown that the total urea output in twenty-four hours cannot be properly compared with any arbitrary finding of urea in the blood at any given moment. For instance, the urea in the blood varies from time to time. We must compare the urine and the blood simultaneously, and all figures must be taken over a fixed period. A good time to choose is a two-hour period after breakfast. If a patient takes his breakfast at 8 A. M., it would be well to make comparative tests between the urea content of the blood and the urea content in the urine at about 10 A. M.

Certain laws have been discovered by Ambard that relate to the output of urea in the urine and its proportion to the urea in the blood. They are as follows:

First, when the kidney puts forth a constant concentration of urea in the urine the total output varies proportionately to the square of the concentration of the urea in the blood.

Second, when, with a constant concentration of urea in the

blood, the subject puts out a variable concentration of urea, the output of urea is inversely proportional to the square root of the concentration of urea in the urine.

Third, or the output of urea (in the urine) varies in direct proportion to the square of the concentration of urea in the blood, and inversely proportionate to the square root of the concentration of urea in the urine.

From these laws Ambard was able to formulate a so-called constant of urea secretion, or, as called by him, the *urea secretory constant*, which may be expressed in mathematical terms.

A. THE AMBARD METHOD

According to Ambard, when the concentration of the urea in the urine is constant, the rate of excretion varies directly as the square of the concentration of urea in the blood. This law is expressed:

$$\frac{(\text{Urea in blood})^2}{\text{Rate of excretion}} = \text{Constant}$$

When the concentration of urea in the blood is the same, the rate of excretion varies inversely as the square root of the concentration in the urine.

$$\frac{\text{Rate of excretion I}}{\text{Rate of excretion II}} = \frac{\sqrt{\text{Concentration II}}}{\sqrt{\text{Concentration I}}}$$

or

$$\text{Rate I } \sqrt{\text{Concentration}} = \text{Rate II } \sqrt{\text{Concentration II}}$$

Introducing this factor into the first law, we have:

$$\frac{\text{Urea in blood}}{\sqrt{\text{Rate of excretion}}\ \sqrt{\text{Concentration in urine}}} = \text{Constant}$$

Other factors remaining constant, the rate of excretion varies directly with the weight of the individual.

$$\frac{\text{Rate}}{\text{Weight}} = \text{Constant}$$

Combining this with the previous formula, we have:

$$\frac{\text{Concentration of urea in blood}}{\sqrt{\frac{\text{Rate}}{\text{Weight}}}\ \sqrt{\text{Concentration in urine}}} = \text{Constant}$$

This formula expresses all of Ambard's laws in the simplest form. In order to standardize the formula for use in human subjects Ambard expresses it as follows:

$$\frac{Ur}{\sqrt{D \times \frac{70}{Wt.}}\ \sqrt{\frac{C}{25}}} = \text{Constant (K)}$$

Ur = Grams of urea per liter of blood.
D = Grams of urea excreted per twenty-four hours.
Wt = Weight of individual in kilograms.
C = Grams of urea per liter of urine.

This formula is known as Ambard's coefficient, and the value of K usually found in the normal human subject is 0.08. The introduction of a standard weight of 70 kg., a standard concentration of 25 gm. per liter of urine, and the expression of excretion as the rate per twenty-four hours are purely arbitrary and do not affect the general relationship between the variable factors. When these arbitrary factors are kept constant, they, in conjunction with the constant relationship between the four variable factors, tend to keep K constant, and the actual numerical value of K is determined by these arbitrary additions to the formula.

Because the formula developed for the expression of this method seems rather complicated, its true simplicity is often unappreciated. Let us pause for a moment to interpret the formula. The coefficient or constant, designated as K, is the same under normal conditions, or is constant in its expression of a distinct relationship between the urea in the blood and the urea in the urine. If the normal figure is accepted as 0.08, we mean that the numerator is but 8/100 of the denominator,

or that the proportion of the figure of urea in the blood as compared with that in the urine—as estimated—is as 8 is to 100.

Index of Urea Excretion.—To obviate the necessity of an arbitrary scale for the interpretation of Ambard's coefficient, McLean has adapted a formula from Ambard's laws based on a scale of 100, so that the rate of urea excretion is given in percentage of the normal, an index of 100 corresponding to a value of 0.08 for Ambard's coefficient.

Procedure.—*Specimens.*—The observations may be made at any time, since the application of the laws is independent of the nitrogen intake. However, it has been considered preferable as a routine to make the observation in the forenoon, no food or water being taken during the period.

The patient is given 300 c.c. of water to drink. One-half hour later the bladder is emptied, by catheter if necessary, and the time noted. Then after one or two hours the bladder is again emptied, the time carefully noted, and the amount of urine measured to within 1 c.c. The shorter period is used when the patient is secreting a fairly large amount of urine. At about the middle of the period 10 c.c. of blood are drawn from a vein into a dry tube containing about 1 gr. of potassium oxalate, with which it is mixed to prevent clotting.

Analysis.—The urease method introduced by Marshall may be used. This depends on the breaking down of urea into ammonia and carbon dioxid by the specific enzyme found in soy bean and the subsequent determination of the ammonia.

Calculation of the index: From the results of the determinations the following calculations can be made:

1. Grams of urea excreted per twenty-four hours = D.
2. Grams of urea per liter of urine = C.
3. Grams of urea per liter of blood = Ur.

Studies made by a number of authors would seem to show that the index of urea excretion gives much more information as to the degree of renal impairment and the prognosis than does the blood urea determination alone.

In general, the phenolsulphonephthalein test parallels the

index of urea excretion; but there are marked exceptions to this rule, in which the phenolsulphonephthalein test apparently gives an erroneous idea of the degree of renal impairment.

B. THE PHENOLSULPHONEPHTHALEIN TEST

This test, which has found much favor in the United States, is both a qualitative and quantitative estimation of the excretion of a given amount of the dye stuff, phenolsulphonephthalein. It may be administered either subcutaneously or intravenously. The latter method is preferable, since the results are then independent of tissue absorption and chemical tissue alteration.

Standard phenolsulphonephthalein is prepared by adding 10 c.c. of 10 per cent. sodium hydroxid to exactly 1 c.c. of a solution of phenolsulphonephthalein solution containing 6 mgm. of the dye and making it up to exactly 1 liter.

Experimental work (Frothingham, Fitz, Folin, and Denis[1]) on rabbits, in which an experimental nephritis had been produced with the injection of uranium nitrate subcutaneously, gave interesting results. The rate of phenolsulphonephthalein in excretion in normal rabbits is about 60 per cent. in seventy minutes. It has been found that in rabbits suffering with uranium nephritis there was but a slight decrease in the phenolsulphonephthalein output, but a considerable accumulation of non-protein nitrogenous constituents in the blood. With a retention of non-protein nitrogen of 216 mg. and of urea 172, there was but slight decrease in the phenolsulphonephthalein excretion. In other experiments the phenolsulphonephthalein output began to improve, while there was still considerable nitrogenous retention. These facts emphasize what was already known, that nitrogenous retention represents the difference between elimination and production or nitrogenous products, while the phenolsulphonephthalein is an indicator of elimination alone. The phenolsulphonephthalein and similar tests give information concerning the renal function at the time the test is made. Although the results may parallel findings in

[1] Frothingham, Fitz, Folin, and Denis, Arch. Int. Med., 1913, vol. xii, p. 145.

blood chemistry, the amount of phenolsulphonephthalein excretion shows merely the renal function for the moment.

The amount of non-protein nitrogen and urea nitrogen in the blood represents rather an estimate of accumulating difference between waste nitrogen as a product of metabolism and the quantity eliminated by the kidneys. A blood chemical analysis would be of greater importance than the outcome of functional kidney tests in prognosis. Cases of almost normal elimination of phenolsulphonephthalein have been reported in spite of marked renal disease (Foster[1]). Extremely low output of phenolsulphonephthalein has been observed with evidently fairly good renal function so far as non-protein nitrogenous retention is concerned.

Estimation of kidney function by determination of the ease and speed with which certain chemical dyes can be eliminated is not always reliable. Because a dye substance is eliminated with a certain degree of facility, we must not conclude that the products of metabolism are excreted in a similar fashion through such kidneys. Regarding phenolsulphonephthalein tests, it has been said that such a test gives a fairly good picture of renal function, but cannot give as reliable information regarding metabolic processes and real kidney deficiency as the blood chemical analysis does.

According to Folin, the phenolsulphonephthalein test indicates the function of the moment, the blood chemical test indicates the true grade of the working power of the kidney. Three important conclusions were arrived at by this author and were corroborated: first, there are many cases with little or no phenolsulphonephthalein excretion that are badly deficient, that show high retention of non-protein nitrogenous blood constituents; second, that there are some cases with decreased phenolsulphonephthalein output that are functioning quite well as judged by the non-retention of these ingredients in the blood; and third, there may be normal phenolsulphonephthalein output with marked retention of blood constituents. From these observations we should hesitate to accept the phenol-

[1] Foster, Arch. Int. Med., 1913, vol. xii, p. 452.

sulphonephthalein findings alone as an expression of the true kidney function. For the urologist the estimation of kidney function from the standpoint of operative risk is not complete unless we include both the percentages of blood constituents and a phenolsulphonephthalein test.

Foster has observed high figures of phenolsulphonephthalein output in patients dying with uremia; or conversely, low phenolsulphonephthalein output in mechanical obstruction in the urinary tract with practically normal concentration of uric acid, urea nitrogen, creatinin, and sugar. In the latter cases the blood chemistry findings are more reliable.

The phenolsulphonephthalein test is also not altogether reliable. In the earlier stages of nephritis Christian[1] finds that the phthalein excretion may be nearly normal and hence of no value. So also Hill[2] reports phenolsulphonephthalein outputs of 60 to 70 per cent. in severe renal damage of chronic nephritis. Indeed, the author thinks that suggestive clinical and physical signs antedate positive findings by either the phenolsulphonephthalein test or with the non-protein nitrogen concentration of the blood. When these two methods deviate sufficiently from the normal, other manifestations are already striking. Even when both tests are negative, we should not conclude that renal lesions are absent. In short, many students of this subject, although admitting the value determinations of the non-protein constituents of the blood in advanced instances of renal functional impairment, are somewhat in doubt as to their value in the recognition of early lesions, particularly of chronic nephritis.

Because of these facts investigations have been made in the value of the injection of test substances that are normally excreted by the kidneys, such as urea.

C. PREFORMED UREA AS A RENAL TEST

The employment of urea as a test substance has found some favor. It is argued that it numbers among its advantages the

[1] Christian, Amer. Jour. Med. Sci., 151, 625, 1916.
[2] Hill, Jour. Amer. Med. Assoc., 75, 596, 1920.

following: first, that it is a product excreted by the kidneys normally and by them alone; second, that it is a true product incapable of alteration within the body; third, that the urea concentration of the blood and tissues may be increased without disturbing any essential physical equilibrium of the body; fourth, the cells of the proximal convoluted tubercles are known to be responsible for the concentration of urea from the blood, and conclusions regarding the localization of functional impairment may be warranted; and fifth, the added stress due to administration of urea may make any latent renal deficiencies manifest.

The modification of the originally proposed methods of urea administration suggested by MacLean and De Wesselow are here given. The test is thus made:

The patient voids, and then takes by mouth 15 gm. of urea dissolved in 100 c.c. of water (flavored with tincture of orange). He then passes urine at the end of one hour and at the end of two hours, both specimens being measured and saved for analysis. The administration of urea induces a diuresis in a few individuals, and should the hourly specimen measure more than 150 c.c., a third hour urine is collected and preserved for the determination. Urea is estimated by the ordinary hypobromite method, a modified apparatus standardized by the more accurate urease method being utilized. The above authors' conclusions, drawn from a study of 1200 cases of war nephritis, indicate that a urea concentration exceeding 2 per cent. means a fairly efficient kidney, and less than 2 per cent. a diseased kidney—the lower the concentration, the more serious the kidney damage.

At the present writing it would appear that the urea concentration test promises to be valuable in the early recognition of renal disease. It must be used, however, in conjunction with other tests, and the data obtained from all carefully compared and weighed.

D. BLOOD CHEMISTRY

Of late years the introduction of blood chemical tests by Folin has opened a new vista and contributed greatly to the accuracy of our interpretation of renal function. Much additional information has been obtainable through studies of retained products of metabolism, as represented by their quantitative estimation in the blood. Indeed, the weight of opinion favors the view today that routine urinary analyses, qualitative or quantitative, are of much less value than a proper appraisal of what ingredients the blood is storing up. While urinary analysis gives us considerable information regarding pathologic conditions in the urinary tract, and concerning deviations in renal function, a complete blood chemical analysis enlightens us regarding the details or minutiæ of renal function.

Of importance in investigations of renal function are quantitative studies of non-protein blood constituents, namely, non-protein nitrogen, urea nitrogen, uric acid, creatinin, creatin, sodium chlorid, and cholesterol.

In nephritis retention of nitrogenous products may occur, sometimes of one ingredient or, again, of all in varying amounts. In early interstitial nephritis the very first evidence of retention of one ingredient takes place in accumulation of uric acid beyond the normal. The normal figures rise from 1 to 3 mgm. up to 4 and 6. Since uric acid is the most difficult substance for the kidney to excrete, and urea occupies an intermediate position, creatinin being easiest to get rid of, the very first interference with kidney function in interstitial nephritis will be arrived at in uric values, then accumulation of urea, and then finally creatinin.

In uremic conditions all three—uric acid, urea nitrogen, and creatinin—may be retained. These observations are of great interest, since they may throw light on the status of the renal organs when the urinary changes are but slight.

The heaping up of these substances is said to be of great value as a prognostic sign, and when creatinin appears in concentration of 5 mgm. per 100 c.c. of blood and over, the case may terminate fatally. In a series of 11 cases reported, in which

creatinin was over 5 mgm., lethal outcome occurred in from a few days to two months.[1]

Whenever gastric symptoms are associated with suspected renal disease, whether with nephritis or renal derangement due to hypertrophy of the prostate or other obstructive factors, the blood chemistry may give important information regarding the true cause of the symptoms. These patients commonly suffer from loss of appetite, flatulency, abdominal distress, nausea, and vomiting—symptoms without relation to meals, but often attended with headaches. Retention of non-protein nitrogenous bodies in such conditions is significant, and careful attention should be paid to the creatinin figures.

The sponsors of the importance of these tests have attempted to show that they are even of value in the differentiation of cardiac from renal lesions. It is often difficult to differentiate between a case that is primarily renal with secondary cardiac symptoms, and one in which the renal derangement is dependent on a cardiac condition. The proportion of urea nitrogen, uric acid, and creatinin in the blood in these cases may throw valuable light on which organ is primarily at fault. The accommodation tests (Strauss, Mosenthal, and Schlayer) described later are also of value in this regard.

The kidneys have a selective affinity for substances delivered to them in the blood, there being a high threshold in the secretion of some substances from the blood, while others pass readily through them.

Attempts to estimate the renal capacity by ability to excrete substances that do not normally pass through the kidneys have not met with unqualified success. The indigo-carmin test, the phloridzin test, and others of this type have been superseded by the more reliable data obtainable from the blood chemistry.

The important functional activities of the kidneys are: 1, Nitrogenous secretion; 2, their ability to prevent acidosis by elimination of acids and retention of alkalies; 3, water and total solid excretion.

[1] Myers and Lough: Arch. Int. Med., 1915, vol. xvi, pp. 536–546.

Too much emphasis cannot be placed upon the correct and trustworthy evidence of blood chemistry figures in diagnosticating nephritis and in making conclusions as to prognosis. Halsey's case may be cited as a typical one, in which the patient, though well enough to visit his physician's office, and with no urinary findings, showed a grave condition in that he had marked retention of urea, uric acid, and creatinin, pointing to a grave prognosis. The case ended fatally within twenty-five days.

The next important function of the kidneys in which the clinician is deeply interested is their ability to help maintain the normal alkali reserve of the body tissues by not only excreting an enormous amount of acid every day (amounting to several hundred c.c. normal acid), but saving bases; *e. g.*, according to Henderson, if the bicarbonates of the plasma were the only method of defense of the body, the organism would succumb to acidosis as soon as the bicarbonate was depleted by the excretion of neutral salts through the kidneys; every molecule of an acid would rob the body of a molecule of bicarbonate. The second mechanism here comes into play and is that by which acids may be removed, leaving behind part of the base with which they have been combined, this base being available for further neutralization. The elimination is by way of the kidneys. These have the capacity to excrete an acid urine from nearly neutral blood. They remove acid phosphate and save base with each molecule of acid phosphate that they excrete. Thus, although alkali is eliminated in the urine, it is much less than would be the case without this specialized kidney activity, and can readily be replaced under normal circumstances by the alkali of the food.

When kidney function is impaired, therefore, acidosis in various degrees may supervene, and this state can be determined by the carbon dioxid tension in alveolar air, by the carbon dioxid combining power of the blood, and by estimating the quantity of accumulated inorganic phosphates in the blood. As a result of a study of a series of nephritics Whitney believed that there are two factors necessary to produce acidosis: failure

of the power of elimination and an increase in the production of acid in the body. Cases with two-hour phenolsulphonephthalein output over 30 per cent. showed acidosis only if there was a severe toxemia, while those below 30 per cent. usually showed acidosis. As causes of increased acid production in nephritis the toxemia of the active parenchymatous form is itself operative; infection is an even more powerful factor.

E. TESTS FOR THE ACCOMMODATIVE OR ADAPTIVE POWER OF THE SEPARATE RENAL FUNCTIONS

These are intended to investigate the response of the kidneys with respect to their ability to excrete water, salt, and nitrogenous substances under varying conditions. For an estimate of the renal function a study of any diminution in the accommodative response or power of the kidneys is of great importance. Thus, the power to concentrate varying substances may be diminished. When such studies are carried out on successive days they become valuable, particularly when they are done to obtain information regarding the water, salt, and nitrogenous output. Estimations of the excretory power of the kidney for water were made many years ago with the cryoscopic method, and both Albarran and Koranyi employed the so-called polyuria test (the inhibition of large quantities of water) to investigate the ability of the kidney to excrete water. It was soon discovered, however, that variations occurred in the kidney's ability to excrete water, salt, and nitrogenous substances. This dissociation was regarded later as being of value in permitting of a differential appraisal of the separate renal function. Therefore, in line with these observations, three sets of tests were evolved for the investigation of these separate functions.

It can be readily understood that the concentrating power of the kidney is of great importance, since when this is interfered with these organs will be unable adequately to excrete the nitrogenous substances and salts, when for any reason oliguria occurs. Under such circumstances, therefore, when either after an operative intervention or by virtue of a diminished

intake of fluid, the output of water is diminished, the deficient concentrating power would tend to the retention of products in the blood.

The results of recent experimental investigations on the etiology of certain histologic components of the kidney have brought to light facts concerning specific function of the various anatomic constituents of these organs. Thus, it is accepted today that water and urea are excreted almost altogether by the glomeruli, and sodium chlorid and salts by the tubules. Clinical observations have led to the opinion that partial isolated derangement of the renal function may occur. These facts emphasize the value of estimates of the separate renal function. Perhaps the most valuable of these is the output of nitrogenous substances, or rather, as the measure of this, the amount of nitrogenous, non-protein substances in the blood.

A number of valuable tests have been proposed, all having in view the study of the response of the kidneys at different times during the twenty-four hours. Normal kidneys react to the stimulating action of certain articles of food, and put out urine in which the specific gravity, nitrogen percentage, and salt percentage vary at different times during the twenty-four hours. In diseased kidneys a certain fixation or inability to vary the concentration of the urine or the percentage of these various substances in the different specimens during twenty-four hours is observed.

The patient is placed upon a standard, well-balanced, mixed diet for a few days. For twenty-four hours the patient is placed upon a special diet. The selected foods are so given as to vary in amount during the day. So also the intake of fluid during the day is varied. The urine is collected at stated intervals during the day, and the night urine is collected as one specimen.

In the test known as the two-hour renal test (Schlayer and Hedinger) the amount of each two-hour specimen, its specific gravity, the amount of non-protein nitrogen or urea, and sodium chlorid are determined, while a similar investigation of the figures for the one nocturnal specimen is made.

Schlayer and Hedinger employ a special diet:

For breakfast: 350 c.c. of coffee with milk and 50 gm. of bread.
Second breakfast: 350 c.c. of milk and 60 to 80 gm. of bread.
Lunch: One plate of clear bouillon, 150 gm. of beef-steak, 150 gm. of potatoes, one roll, one cup of coffee.
Afternoon: 350 c.c. of coffee and 60 to 80 gm. of bread.
Supper: 500 to 600 gm. of cereal.

The urine is collected in two hourly portions, and the night urine collected from 9 P. M. to 7 A. M. in one portion.

In each portion the quantity, specific gravity, and sodium chlorid concentration are estimated.

In the healthy person minimal variations occur in the quantity, specific gravity, and salt concentration by reason of the influence of the diuretic food substances. Further, the total urine is greater during the day than at night in the normal.

The specific gravity should vary among the different specimens over a range of about 10 points, and in some of the specimens it should be 1018 or over. The total nitrogen should approach within a few grams of the total nitrogen in the diet, and variations should be observed in the percentage of the non-protein nitrogen, indicating that it may be secreted at varying concentrations. Such variations in percentage are usually small. The same applies to the excretion of sodium chlorid.

In disease of the kidneys the amount of night urine may exceed that of the day, and the specific gravity may show little variation in the different specimens. This is known as fixation of gravity, and may be at a low level or at a fairly high one. There may be inability on the part of the kidney to vary the concentration of one or the other of the constituents. Since this test gives data in regard to the special ability of the kidney to put out water, nitrogen, and salt, it is of distinct value in outlining the treatment.

The Strauss Method for Test of Accommodative Power.—The following is modified from Strauss and may be found useful. On the evening before the examination the patient receives 2 eggs, 1 gm. of salt, a roll with butter, and 200 c.c. of tea,

being advised not to take anything during the night. On the day of the examination the patient voids at 6 A. M. and again at 7 A. M., the specimens being preserved. Thereupon the patient drinks 1 liter of weak tea and is advised to void every hour for four hours without taking anything by mouth during this period. At 11 o'clock he receives 100 gm. of bread (white), 100 gm. of cheese, and 1 gm. of salt. At 1 P. M. the patient receives 3 eggs and 1 gm. of salt, 1 apple or an orange. At 4 P. M. again 100 gm. of white bread, with 100 gm. of white cheese, and 1 gm. of salt. The patient voids at 11 A. M., 1, 4, and 7 P. M. Thus, the specimens are at hand taken at the following periods: 6, 7, 8, 9, 10, and 11 A. M.; 1, 4, and 7 P. M. The quantity, the specific gravity, and percentage of salt and urea are estimated in each portion. Experience shows that the height of the polyuria or dilution usually takes place during the first two or three hours after inhibition of fluid, and the height of the concentration after taking the dry diet, usually in the hours between 4 and 7 P. M. Whenever there is delay in the fluid output, it may be necessary to prolong the concentration experiment in such a manner that on the evening of the experimental day a dry supper is given, just as on the evening preceding the test. Specific gravity is then taken at 10 P. M. in such a case, as well as on the following morning at 6 and 7 A. M.

The normal individual on such a régime usually puts out about 1200 to 1400 c.c., most of the fluid being excreted during the first four hours. Its specific gravity drops in the first two or three hours to 1002 to 1004, and after five or six hours, as a rule, the original specific gravity is attained. During the period of the dry diet, in the latter part of the afternoon, between 4 and 7 P. M., its specific gravity may rise from 1025 to 1030. If under pathologic conditions the specific gravity fails to rise to 1025 by 7 P. M., it may, if the experiment be protracted, attain this figure by 10 P. M. or on the following day. If the excretion of the imbibed fluid is complete within four to five hours and in almost equal hourly portions without much variation in specific gravity, evidences of functional derangement are at hand.

An excellent idea of the practical reading of results can be

obtained from a perusal of characteristic charts published by Strauss himself.

A *normal* case is here given:

Time.	Urine in c.c.	Specific gravity.	NaCl per cent.	U. per cent.
6	350	1020	0.48	1.56
7	25	1030	0.71	2.40
Total 1000: 8	140	1008	0.24	0.54
9	500	1003	0.06	0.39
10	270	1002	0.06	0.39
11	90	1010	0.24	0.66
1	40	1020	0.48	0.79
3	45	1026	0.65	0.92
5	85	1025	0.59	1.32
7	30	1031	0.83	1.56

Total.....1200 Min...1002 Min...0.06 Min...0.36
Max...1031 Max...0.83 Max...2.40

Total nitrogen: 24 mg.

In chronic glomerular nephritis excessive and prolonged diuresis are exemplified in the following table:

PROLONGED AND INCREASED WATER OUTPUT

Time.	Urine in c.c.	Specific gravity.	NaCl per cent.	U. per cent.
6	190	1028	0.80	0.39
7	32	1026	1.29	1.8
Total 1294: 8	224	1006	0.56	0.42
9	630	1002	0.12	0.09
10	340	1004	0.16	0.12
11	100	1012	0.94	0.18
1	100	1022	1.10	0.75
4	165	1020	1.12	0.09
7	152	1028	1.43	0.45

Total.....1711 Min...1002 Min...0.12 Min...0.09
Max...1028 Max...1.43 Max...1.8

Total nitrogen: 36.5 mg. Blood-pressure: 80/115 mm. Hg.

Interpretation of Strauss Method.—We must take into account that readings of specific gravity, sodium chlorid, and urea percentages are dependent in great degree on the simultaneous excretion of water. When there is delayed water excretion, low figures for the specific gravity, salt and urea during the afternoon period do not necessarily mean a severe degree of renal insufficiency. Strauss suggests that a condition of "pseudohyposthenuria" may obtain. For the diagnosis of a severe degree of renal insufficiency there must also be a coincident marked *oliguria*. By continuing the test over a longer period and by limiting the fluids (dry diet) during the evening of the test day, or even during the consecutive night and following day, a more reliable survey of the concentrating power can be arrived at if the urinary findings be correspondingly followed up.

Of most importance is a comparison of the minimal and maximal values in evaluation of renal accommodative latitudes or capacity, and of the diuretic and concentrating powers. Single figures may be influenced by previous nutritional conditions and so may vary in repeated examinations. The rapidity and extent of accommodative power are of greater importance than a view of the total capacities of the kidneys. A comparative appraisal of various methods of investigation is more reliable than conclusions based on a single test.

Data on Sodium Chlorid Concentration.—As an index of the renal working capacity the maximum point in sodium chlorid excretion is also of importance. The minimum quantity is of little import as compared with the minimum specific gravity point. The maximum salt output gives us information as to the height of concentrating power of which the kidney is capable. The maximal value may reach the figure of 1 per cent. or even more. If the percentage of salt output shows but slight changes from hour to hour and does not exceed the maximal value of 0.3 per cent., one can conclude a deficiency in the excretory function for salt. Although very frequently such restricted capacity for salt output is attended with a generalized renal deficiency, dissociated functional derangements are not infrequent.

The Urea Output.—Here, too, the maximal figures are of

most importance. In the healthy person the percentages are usually between 1 and 2 per cent., varying somewhat with the nutritional conditions. With reduced protein intake histogenic retention of nitrogenous substances may take place that may stimulate renal insufficiency. Such a condition was noticed during the Great War, when abnormally low percentages of urea in the urine were observed in soldiers and in the undernourished.

Concerning the Interpretation of the Results of Accommodative Experiments.—The quantitative values obtained in these tests are only reliable when the patient is free from metabolic disturbances, such as edema, and when the metabolism is in an approximate balance. We should compare the minimal and maximal values as expressive of the latitude of renal response or of the ability of the kidneys to concentrate or dilute. The total quantitative figures for the products of excretion are not important, since these depend upon the diet, and are metabolic rather than renal questions. The rapidity and the latitude of the renal response is more important than the total function. Indeed, these simple experiments together with the findings of blood chemical analysis will suffice to give an excellent idea of renal function. Only repeated and synchronous applications of a number of tests can give a correct insight into the nature and capacity of the renal activity.

F. TESTS OF MAXIMUM CONCENTRATION

The term *maximum concentration* was introduced by Ambard, and frequently employed by Legueu and Chabanier in their work on renal function. In describing the composition of urine one may speak of the total concentration (concentration globale), meaning thereby the percentage of all the solid substances excreted and dissolved, or we may refer to the concentration of individual or separate substances excreted. In the study of maximum concentration it is customary to refer to a single substance. In this manner the power of the renal parenchyma to concentrate may be analyzed in the most simple fashion. It is only after we have obtained an idea as to the

manner in which the kidney concentrates a single substance that we can properly appraise the power to concentrate a number of substances simultaneously. It is well known that the maximum concentration with which a kidney is able to excrete one substance is roughly indicative of its capacity in the matter of other substances. The substance of choice for such study is the urea.

The Maximum Concentration of Urea.—Certain special diets have been suggested to cause a progressive increase in the concentration of urea in the urine up to a maximum percentage. Beyond this the urea concentration remains stationary even though the diet be continued for a longer period or even increased in amount. The maximum percentage thus obtained is *the maximum concentration of urea.*

Technic.—The patient is made to take daily the coagulum of 3 to 4 liters of milk from which the whey has been taken off, and to which sugar has been added. This milk is made to curdle by the use of rennet and then filtered through muslin. Powdered sugar is added to the coagulum in the proportion of about 30 gm. to the liter. To this flavoring may be added as desired. This semisolid coagulum is taken during the first two days without any fluid, and toward the third day the patient is allowed to take mouthfuls of water to quench the thirst. This diet is one very poor in chlorids and water. It causes urea to be put out in large quantities and does not produce immediate thirst.

Experiments have shown that the maximum concentration is obtained automatically during the third twenty-four hours, and usually amounts to 53 to 56 gm.

Experiments by Ambard, carried on by limiting the water intake in patients who have received the augmented protein diet, demonstrated that the kidneys cannot concentrate urea above a certain level. It would appear possible to augment artifically the concentration of urea in the course of an excessive protein diet by restriction of water. However, it is found that although the urine diminishes in volume the concentration does not vary above the point previously regarded as the maximum. It is found that the urea in the blood may increase considerably.

In spite, therefore, of the restriction in water intake, the concentration does not increase and the patient accumulates urea in his system. It has been found that the maximum concentration of urea is independent, first, of the quality of urea eliminated; second, of the other urinary components that are simultaneously excreted; third, of the quantity of the renal parenchyma; and fourth, of the nervous system.

As for the relation of the maximum concentration (urea) and the simultaneous excretion of other substances, observations seem to indicate that the renal power of concentration is not the sum of the total activities of the renal organs, but that the latter apply themselves to the excretion of each substance with a special concentrating power. Thus, when the kidney is exhausted in its power to concentrate urea (having attained a maximum), it can be induced even then to increase its power to concentrate chlorids. Thus, although there is a maximum concentration point, we cannot speak of a total sum of maximum concentration.

The maximum concentration is independent of the quantity of renal parenchyma. In experiments conducted after a nephrectomy the maximum concentration was found to have been regained forty-eight hours after the removal of one kidney, long before compensatory hypertrophy could have taken place.

As for the rôle of extrarenal nerve factors, it was found that dogs in whom the renal nerves had been severed could concentrate urea just as well as before the operation.

Is the maximum concentration an expression or measure of the quality of the renal parenchyma? It must be remembered that not every deterioration of the renal cells must needs be translated into a decline of the concentrating power. In fact, the renal cells have another function not less important than the concentrating power, namely, that of regulating the threshold of excretion. The concentrating power and this latter activity, that of varying the threshold, may be independently affected. Therefore we must not conclude that every renal lesion must manifest itself necessarily in a diminution of the maximum concentration.

THE INTERPRETATION OF FUNCTIONAL TESTS

A. **General Interpretation.**—While the urinary findings, when interpreted in the light of a measure of function, are fortuitous and to a certain extent dependent upon the particular conditions that may obtain on the day of examination, the composition of the blood-serum is not so apt to undergo such great fluctuations. There is considerably more stability, therefore, in data obtainable through the latter method of investigation. The findings obtainable from a study of the blood-serum as indicative of the activity of renal function must be given a higher rating than what is deducible from the urine alone.

If all the results obtainable from the various renal functional tests are taken into consideration, it will be noted that there is not always a parallel between the anatomic and functional conditions of the kidney. We must not attribute too great importance to minor deviations from the normal. Alterations or changes of slight degree may be of neurogenic origin. There are cases on record where marked histologic changes were found in the kidneys postmortem, while the functional tests were practically normal.

It is furthermore known that anatomic defects in the kidney can be compensated for through vicarious interposition of such other mechanisms that act in a compensatory manner. The cardiovascular system is one of these.

The best concept of the functional condition is obtained not only if we employ a number of methods at the same time, but by frequent repetitions of the procedures. Several tests are necessary for a proper estimation of the renal work, and it is futile to attempt to seek in one test a method that is adequate to estimate the capabilities of an organ of so many activities. At best we can expect only to gain information concerning disturbances in certain biologic systems when we apply methods of functional investigation.

To make correct deductions regarding anatomic pathologic alterations is difficult. It may be possible to glean something in this regard through a combination of examinations. Such would include studies of water, sodium chlorid, and nitrogen excretion.

But in accepting the value of any of the tests for accommodative power of the kidneys it must be remembered that the non-nitrogenous products of the blood are of the greatest significance. The excretion of dyes also is inferior in value to the blood examination.

In judging the value of functional tests one should distinguish between direct retention and indirect retention of products in the blood. Retention of nitrogenous substances may be due to a deficiency in function of that particular portion of the kidney usually responsible for this substance. When such is the case Strauss speaks of a *specific type of retention.* However, in indirect fashion the same result may ensue when by virtue of a marked degree of oliguria, or even anuria, nitrogenous products are retained. This latter may be called *general retention.* In spite of good excretory power, according to Strauss, the nitrogenous products may reach high values in the blood, even up to 120 mg. or more of total nitrogen, when oliguria has been present for some time. Or, by virtue of cardiac insufficiency in renal sclerosis, a sudden increase in the nitrogenous values may be observed. Therefore we must conclude that excretory power and actual excretion or excretory values are not identical concepts.

Oliguria points to an insufficiency of the glomeruli if we accept the view that excretion of water takes place only through the glomeruli. Cardiogenic and nephrogenic oligurias may be differentiated, however, in that the renal concentration power is not interfered with in the former. According to Strauss, where there is a combination in cases with renal insufficiency difficulties may arise. In cases of polyuria with coincident diminution of the activity of the kidney conclusions may also be difficult, and abnormally diluted urine can be the result of abnormal diminution in the amount of solid substances (particularly sodium chlorid) and due to secretory insufficiency (adynamic type). Or this may be due to the result of abnormal irritability of the vascular apparatus (erethistic or irritative type). The former type can be recognized in that accommodation experiments with salt solution (sodium chlorid) are followed

by abnormally low concentration, giving the experimental phase. In the latter case, with vascular irritability, considerable increase in the salt excretion will occur during the experimental period.

B. **Interpretation in Urologic Surgery.**—The problem of correctly interpreting the importance of renal function in urologic surgical work should not confine itself to estimates of prognosis, but should concern itself especially with operative indications. Therefore, all of the factors that could influence the outcome of any surgical intervention must be properly weighed, and the case in hand studied with the following questions in view:

(*a*) Did the patient have
  (1) Normal kidneys?
  (2) Kidneys the seat of a chronic nephritis?
  (3) Kidneys the seat of an anomaly, aplasia, congenital maldevelopment?

(*b*) Is the surgical lesion unilateral or bilateral?

(*c*) What effect does a toxic absorption from the diseased kidney exert on the integrity of the healthy organ?

(*d*) What is the influence of inhibition on the secreto-excretory power of the healthy kidney?

(*e*) What rôle may the superadded factor of surgical intervention play in upsetting the balance of already adjusted renal function?

(*f*) What can we expect in the sense of an amelioration of renal function through the effects produced by operation?

(*g*) To what extent is the patient already calling upon compensatory forces to make up renal deficiency?

(*h*) What is the condition of the cardiovascular system and its relationship to the existing totality of renal function?

(*i*) What may be the effect of bleeding, shock, infection, anesthesia, and the other coincident stresses and cardiac strains ushered in by a surgical procedure?

These considerations make the problem a complex one, in which mathematical results and absolute quantitative figures

must receive only a subordinate place in the total evaluation of the patient's capacities.

The limitation of any single functional method of examination when taken at one time, or alone, is well known to the experienced urologist. Neither the phenolsulphonephthalein test, the absolute figures obtained from a study of the blood chemistry, nor any single feature is a reliable estimate of the functional capacity of the renal organs, and certainly does not give accurate data regarding the pathologic alterations and the extent of destruction that may have taken place in one or both kidneys. A few examples will illustrate:

S. B., a young man thirty-five years of age, presents himself with an enormous hydronephrotic kidney on the left side occupying a large part of the left half of the abdomen, ureteral catheterization demonstrating the existence of pus and an obstruction at the ureteropelvic junction due to stone. The other kidney is three times the normal size, hydronephrotic, contains multiple stones, and is infected.

Although the phenolsulphonephthalein test varies from time to time from 0 to 10 and 15 per cent. in two hours, the blood chemistry was found consistently within the normal during a certain period.

Although this particular individual found himself in a state of balance as far as renal function was concerned, it is evident that in spite of the absence of any retention of nitrogenous products in the blood on several examinations the patient's renal function was reduced and inadequate.

After a nephrotomy was done on the left kidney under local anesthesia the function of the right kidney improved considerably, so that the phenolsulphonephthalein test indicated an advance of 10 points, up to 20 per cent. or slightly over, and the general condition of the patient improved by reason of the evacuation of pus and the elimination of toxic absorption.

Were we to regard the low figures, such as a zero output of phenolsulphonephthalein, as indicative of contraindication to operation, we would fail to help many of the patients who are not only improved, but cured, by surgery. In the cases

of prostatic hypertrophy we not infrequently find a zero output of phenolsulphonephthalein over a period of one or even two hours, or minimal quantities from 0 to 10 in patients who under conservative careful surgery not only withstand the preliminary suprapubic cystotomy for drainage but also permit of the extirpation of the prostatic adenoma with little or no complications.

The following interesting case of bilateral Bacillus coli pyelonephritis in a young woman with kidneys already damaged by reason of the existence of a chronic nephritis, will illustrate how little reliance can be placed upon the failure of a dye, such as phenolsulphonephthalein, to be excreted.

S. K., a young woman thirty-three years of age, who had been threatened with uremia during the eighth month of her pregnancy, was delivered prematurely, and shortly thereafter developed what was considered a pyelitis. She ran constant temperatures for about four to five weeks, and when she came under my observation there were evidences of the existence of a bilateral pyelonephritis, with temperatures ranging between 102° and 103° F. Although the phenolsulphonephthalein output was zero, it was decided to decapsulate and drain one kidney, and then later on it was found necessary to do a similar operation upon the other side.

Both kidneys were found extensively diseased, at least two-thirds of the parenchyma of each organ being converted into suppurative areas. Some two months after the patient's admission to the hospital the patient's phenolsulphonephthalein output had risen to 32 per cent. It may be said, however, that there was no retention of nitrogenous products in the blood when her phenolsulphonephthalein test was zero.

This case demonstrated beautifully how unreliable the dye tests are as an index of the patient's ability to withstand surgical procedures on the kidney.

When we come to a consideration of the figures obtained by blood chemical analysis, we will note that a high urea nitrogen, high incoagulable nitrogen, and even creatinin of 4.8 to 6.3 and over do not necessarily indicate an early or immediate

lethal outcome, even though very high figures are recognized as being of very grave import. Thus, the following case of contracture of the neck of the bladder with chronic retention and chronic cystitis, with attacks of pyelonephritis and chronic pyelitis is an example:

J. M., male, fifty-eight years of age, had a zero output in January, 1921, and the blood chemistry gave the following figures on two different occasions: urea nitrogen, 62 and 54.6; incoagulable nitrogen, 120 and 128.9; creatinin, 4.8 and 6.3, and uric acid, 6.

In spite of these high figures suprapubic cystotomy under local anesthesia was done. Although the patient was very sick at the time of operation and continued desperately ill for some three weeks, he gradually recovered so that he remained well and under observation with his suprapubic drain *in situ* for somewhat over a year, when in July, 1921, some six months after the operation was performed, the non-protein nitrogen figures were as follows: urea nitrogen, 25.2; incoagulable nitrogen, 70; creatinin, 3, and uric acid, 4.3.

About fourteen months after operation the patient finally succumbed in an attack of uremia.

It is evident here that, although the prognosis was grave, the patient's life was prolonged for about fourteen months through a conservative operation in spite of the high nitrogen figures in the blood and the zero phenolsulphonephthalein.

What interests us most in surgical practice is the bearing that renal functional tests may have on the operability of any given case, and for practical purposes we may divide the cases in which operative indications must be made in the following way:

A. Operations on the lower urinary tract including the bladder and the prostate; and

B. Operations on the kidney:

(1) Operations on the lower tract include particularly

(*a*) Prostatectomy for hypertrophy of the prostate (adenoma), and

Resection of the sphincteric region for contracture of the neck of the bladder.

(*b*) Resection of the bladder for carcinoma and resection of the prostate for carcinoma.

(2) Operations on the kidney may be divided into those requiring

Incision and drainage (nephrotomy and nephrolithotomy), or
Pyelotomy or pyelo-ureterotomy, or
Decapsulation with or without nephrotomy, and
Those requiring removal of the kidney (nephrectomy).

OPERATIONS ON THE LOWER URINARY TRACT

Here it must be remembered that the function of the kidney may be improved by catheter drainage or cystotomy, and that an intervention must be interpreted rather in the light of an ameliorating factor than as an added renal stress so long as the immediate strain induced does not disturb the equilibrium previously established.

(*a*) **Prostatectomy for Hypertrophy.**—The functional findings as estimated by phenolsulphonephthalein output or by the accumulation of nitrogenous products in the blood may be misleading, for they represent merely temporary inhibition of the function, or temporary retention of waste products due to faulty kidney and bladder drainage. And these may be ameliorated by bladder drainage through suprapubic cystotomy under novocain local anesthesia. So, in the case cited above, where the phenolsulphonephthalein output for a long period was zero, and the nitrogenous waste products and incoagulable nitrogen were more than double the normal, with temperature over a considerable period, pyelonephritis and a suburemic state, suprapubic drainage was followed by marked improvement of the kidney function up to 43 per cent. phenolsulphonephthalein and simultaneous reduction of the blood values.

(*b*) **Carcinoma of the Bladder.**—Here we should distinguish between three types of cases: first, those causing obstruction at the neck of the bladder, carcinoma of the neck involving the prostate with obstruction; second, those situated in mobile portions of the bladder, vertex, posterior and lateral walls,

without causing obstruction, but causing hematuria; and third, those about one ureter, either originating in the ureter, with blockage and exclusion of the corresponding kidney, or secondarily closing a ureter.

Carcinoma of the bladder involving the neck presents a problem similar to obstructions due to other causes, hypertrophy of the prostate and prostatic adenoma and carcinoma, and requires relief of the obstruction, some, being operable, permitting of resection. Others are inoperable, but require alleviation of the vesical symptoms by drainage with or without the use of radium. Here the same factors obtain as in obstruction due to other causes, stricture and prostatic adenoma, and relief may be obtained by suprapubic cystotomy and consequent improvement of the renal function.

Carcinoma Elsewhere in the Bladder in Its Mobile Portions.—Here, because of the hematuria, catheterization of the ureters may be necessary for a proper estimate of the phenolsulphonephthalein output and of separate renal activities. The urine is to be collected over two-hour periods. The Ambard coefficient as well as the nitrogenous portions of the products in the blood give valuable information. When there is no obstacle to the outflow of urine, the blood chemistry values, the Ambard coefficient, and the phenolsulphonephthalein output may be interpreted as correct, since they are not influenced by obstructive bladder conditions, such as stricture, prostatic adenoma, and prostatic carcinoma.

Carcinoma of the Bladder or Lower Ureter Causing Closure of the Ureter in the Bladder and Exclusion of the Kidney.—Here, too, because of blood in the urine it will be necessary to estimate the function of the other kidney from two-hour collection of urine direct from the ureter, and using the phenolsulphonephthalein, blood chemistry, or Ambard coefficient as our guide. When the phenolsulphonephthalein figures are low and the Ambard and blood values high, extensive operation and resection will be contraindicated. Here, too, the exclusion of one kidney for a long period of time may have had a deleterious effect upon the other kidney. Pyelonephritis of the supposedly

healthy organ without symptoms may still further reduce the remaining and impaired function.

Our own recent work on the treatment of carcinoma of the bladder with radium, either through the cystoscope or by the suprapubic route, has considerably reduced the mortality. For, when a small carcinoma involves the ureteral orifices, the implantation of radium emanations as a preliminary step either completely destroys the carcinoma or so thoroughly necroses and inhibits its extension, that resection may be done as a second step with greater ease and less stress upon the surviving kidney if and when deemed indicated.

In carcinoma of the bladder or carcinoma at one ureteral orifice, and where the act of micturition is not mechanically impeded, the kidneys do not gain anything through an operation on the bladder. Hence all renal functional values must be taken as at their maximum, and the risks weighed accordingly.

OPERATIONS ON THE UPPER URINARY TRACT

Where we are dealing with nephrotomy, the problem is quite different from that of nephrectomy.

Two types of nephrotomy deserve consideration in this connection, nephrotomy in cases with marked distention of the kidney and reduction of the cortical substance (uronephrosis, pyonephrosis, and hydronephrosis), and nephrotomy where the quantity of renal parenchyma has suffered but little. Paradoxically, relatively more is to be expected from an operative procedure on kidneys whose parenchyma has been reduced considerably, for the risks are relatively slight when such kidneys are incised for purposes of drainage. It must be remembered that other factors besides the operative shock and the anesthesia enter into the total composite insult inflicted by an operation. And in the case of nephrotomy it is secondary hemorrhage and the injury to the renal parenchyma that may be such important factors as to reduce materially the benefits that should accrue to the patient. In other words, since hemorrhage, secondary necrosis, or infarction due to drainage are not to be feared where marked hydronephrosis is present, the

relative risk of nephrotomy in such kidneys is slight. *Therefore, when we appraise the chances of recovery by an estimate of the functional activity of the kidneys alone, we are prone to misjudge the circumstances unless we take into account the factors above mentioned.*

Because nephrotomy with or without decapsulation may reduce the results of infection by abolishing retention of pus and toxic absorption, and since it can be carried out with no shock, it is an operation which can be expected to improve either the kidney upon which the operation was performed, the other kidney alone, or both. By the same token it is followed by amelioration of renal function.

In the case of nephrectomy these effects do not obtain to the same degree, although the reduction in amount of the circulatory toxic substances and of the abatement of infection are factors that may also play a rôle in improving the sister organ. Nevertheless, nothing additional is contributed in the way of function, but merely inhibiting and impeding forces such as cause deterioration and impairment, are eliminated.

The Significance of Indications of Poor Function in the Problem of Nephrectomy.—As already alluded to, the existence of data indicative of poor renal function must be interpreted in the light of a number of qualifying or modifying circumstances. Legueu cites the following:

(*a*) The effect of the lesion in the diseased kidney upon the healthy one in reducing its function.

(*b*) The rôle of the diseased kidney and its capacity to contribute toward the total function.

(*c*) Whether an operation on the lower tract will raise the total function of both (for complicating stricture, cystitis, carcinoma, hypertrophy or adenoma of the prostate, contracture of the neck of the bladder, etc.).

(*d*) The difficulties presented by the operation and the shock that would be inflicted in the particular case at hand, as determined in a given case by the size of the tumor (in hypernephroma, carcinoma of the kidney), the size of the infected kidney (hydronephrosis, pyonephrosis), the extent, vastness,

and hardness of the adhesive process about the kidney and ureter, its adhesion to the peritoneum; the loss of blood that would be entailed, etc.

(*e*) The general condition of the patient, the heart, the blood-pressure, the metabolism, and the lungs.

(*f*) The insignificance of the mass to be removed as a contributor to the excretory forces of the organism. Are we to operate upon a functioning organ or a destroyed organ, which at the time of intervention can be regarded in the light of an infected or foreign body, no longer of physiologic worth?

The Importance of the Estimation of the Renal Function when Nephrectomy is Necessary.—The determination of the functional value or worth of the healthy kidney is of as great importance as the recognition of which organ is diseased.

Let us not for a moment believe that the last word has been said in this vital and intricate problem; and let us, therefore, approach the subject with an open mind, taking for some worth, at least, observations of other schools of thought. Although a decision as to the operability of cases is in most instances easily made by the experienced urologic surgeon, instances do occur in which by virtue of the bilateral nature of the lesions we should resort to a number of methods to clarify our tenets.

The French school,[1] laying great stress on the value of the Ambard figures, have recently expressed themselves regarding the renal functional methods in the following way. A brief résumé may not be amiss.

Ureteral catheterization as a method to evaluate function of the healthy organ is now considered subsidiary in value to functional tests. The French school still makes functional tests, however, by leaving the ureter catheter *in situ* for two hours with the following in view: to estimate the polyuria test, the quantity of fluid excreted, the concentration of urea and chlorids, the percentage of urea and chlorids, and the maximum output.

(*a*) The *volume of fluid excreted after the polyuria test* is no longer considered so important as formerly by Legueu, since

[1] Legueu, Ambard, Chabanier, etc.

it has been found that water excretion may be defective in the case of a good kidney. No deduction can be drawn from *poor* response to the polyuria test. Only a good response on the part of the supposedly healthy organ.

(*b*) *The Concentration of Urea and Chlorid.*—Random specimens are also of little functional value. Figures such as 12 to 20 gm., ordinarily regarded as sufficient, may be insufficient, while very low figures (3, 4, or 5 gm.) may be associated with adequate renal function. The same holds good for the total output in grams. Ordinarily 1 gm. of urea in two hours would be regarded as favorable. It would not be held so if the water output were very scant, and still even in such cases the kidney function may be good.

(*c*) The *maximum output*, or the highest concentration obtainable in two hours multiplied by the greatest output of water within any half-hour period, is of more value. Although all of these tests are of some value, they are not absolutely reliable.

More recently the study of the Ambard coefficient has given results that are more in accord with clinical results, and quite at variance with the findings of other means. Figures that would warrant the conclusion of bilateral renal impairment, and that would make us reject operative intervention, when put to the test of the Ambard method not only give proof to the correctness of intervention, but find confirmation of their value in clinically good results.

Quite contradictory may be the results of the various tests. For instance, Legueu reports the following:

Urea concentration, 25 gm. to the liter; output in grams, 5 gm. of urea in two hours; polyuria test, 175 gm.; that is, favorable figures warranting operation.

Az (nitrogen) 0.85 or K : 0.176, these figures quite at variance with the above, and contraindicating operation.

Operation by another surgeon was followed by renal insufficiency and lethal outcome.

Another case quoted by the same author, as follows:

Healthy kidney, 151 gm. of water in two hours; concentration 3 gm. in the first half-hour and urea in two hours 0.41,

or figures that could be regarded as too low. These were associated with an azotemia (Az 0.25), and a constant (Ambard) or K : 0.062, which figures contradicted absolutely the above, and spoke for adequate renal function.

Such examples demonstrate that absolute excretory values *per se* have but limited significance. The output of water and solid substances must needs be valued not in comparison with what a normal individual excretes, but rather in the light of what defective kidneys should put out in order to detoxicate blood that may be overloaded with poisonous products.

While the usual functional methods seem to offer some security, they do not give absolute guarantees. An analysis of the urine permits only of the appreciation of the functional activity of the kidney at the moment, and gives no clue as to the relationship between that which goes into the kidney and that which is excreted. And thus a ratio between the values in the blood and those in the urine is essential for a correct estimation of renal function.

The Application of the Ambard Constant.—The most recent views of the French school may be summarized as follows: When the coefficient gives a figure below 0.100 and one kidney is involved, the function of the supposedly healthy kidney is presumably adequate, provided it has been established as being without surgical lesion by proper cystoscopic and radiographic methods.

When the constant is over 0.120, one must be guarded, as it is an empirical deduction that with such a coefficient or one higher, the case is within the realm of doubtful risks. In general, it may be said that as one approaches a constant of 0.140 it is still possible to effect a cure with nephrectomy, although the dangerous features increase *pari passu* with increasing constants.

Another important factor to be taken into consideration is the distribution of the renal lesions; and this applies to whatever functional tests we rely upon. With the same values and with the same high Ambard nephrectomy may be permissible or contraindicated, depending upon the relative participation

of one or both kidneys in the surgical lesion. The higher the constant, the more necessary is it to find extensive destruction of one kidney, for the removal of a more or less completely destroyed kidney should hardly alter the total capacity. Even with a high constant, if the kidney contribute little or nothing to the total renal function, the healthy side may still be adequate, provided the operation be not too bloody, the anesthesia not too prolonged, and too much infection be not introduced.

Where, however, the kidney removed has been a contributing factor to the combined renal function and of considerable value, the consequence of nephrectomy with a high constant may be grave. The function then may be reduced to a degree incompatible with further life.

In other words, in the interpretation of the high constant or of any one or combination of tests, by the removal of the small quotum furnished by the diseased organ, a high degree of clinical sense is necessary, for numbers alone will not serve. The experienced urologist may instinctively know that the high constant or other doubtful figures correspond only to the sum of the lesions, reflex and toxic effect produced by the diseased kidney, and correctly interpreted, kidneys may be removed in the presence of very dubious figures.

It is in the cases where we find ourselves in dangerous zones (high blood and Ambard values) that bilateral ureteral catheterization with relative evaluation of the output of the two kidneys may be of extreme importance. For, should we find that the diseased kidney excreted a relatively large percentage of the total, or little less than the healthy side, in a case of high blood and Ambard values, nephrectomy would be deemed inadvisable. When the diseased kidney, however, contributes but little, and the urea concentration is very feeble, one may be sure that its removal will barely affect the outcome.

Let us now put the question always in the minds of those whose practice has given them but a restricted viewpoint as to the latitude of expectancy from any or all of the functional tests, namely, What are the figures, if any, that will under all circumstances contraindicate operative intervention on a kid-

ney, be this nephrotomy or nephrectomy? The answer must be, Figures alone cannot decide the point for us.

While the French school may hesitate to operate in the face of an Ambard above 0.140, we have successfully done nephrectomy with an Ambard of over 0.2, and with a Mosenthal test showing marked renal inadequacy. In other words, an operation such as nephrectomy when rapidly done, and without the loss of too much blood, with the removal of a kidney that contributes naught to the renal work, has been found possible in the presence of figures that would be expected to be critical. It is just that the toxic factor said to inhibit the action of the healthy kidney whose elimination may outweigh or counterbalance any deleterious elements injected by an operation. Its degree is inestimable by any means other than pure clinical appraisal.

Complicating Factors in Postoperative Renal Function.—The French observers speak of a veritable acute nephritis that may follow operative intervention, at least in the functional sense of the word. There follows a rapid fall in the concentration of the urine, and with this an increase in the nitrogenous retention. This condition may supervene in subjects whose kidneys apparently functionated well before operation (as well as in cases where function was more or less diminished before operation).

After operation one observes at times a fall in the water output and simultaneously an increase in the concentration of urea in the urine up to a certain percentage, above which it cannot rise. This point represents the maximum concentration of the urea in the subject under consideration. From this moment on the quantity of urea eliminated is dependent upon the urinary volume. That is to say, as long as this volume is insufficient to eliminate the urea elaborated in the organism, the latter must accumulate in the blood. Therefore, nitrogen retention after operation will be apt to occur in proportion to the duration and intensity of the restriction of urinary output. But even in cases with markedly altered kidney excessive retention in the blood may not occur after operation provided sufficient amount of water is put out.

According to Chabanier[1] toxic and non-toxic urea should be distinguished.

Two types of cases are observed which do not express a constant relationship between the intensity of the nitrogenous retention and the clinical symptoms. By this we mean that in certain cases there is considerable accumulation of nitrogenous products without clinical phenomena, while, on the other hand (according to the French authors), subjects with an azotemia no greater than 2 or 3 gm. succumb with toxic symptoms.

CONCLUSIONS

From what has been said it will be readily appreciated that to the phenolsulphonephthalein we must relegate but a subordinate place because of the inadequacy and unreliability of the information furnished by it. A low phenolsulphonephthalein output indicates merely the inability of the kidneys to excrete the dye at any given moment. Such findings do not tell us what the kidneys could be made to do, or whether the patient is not in a good functional balance or equilibrium. Even in the presence of minimal quantities of phenolsulphonephthalein output less than 15 per cent., the renal organs may be excreting adequately as far as the waste products are concerned that are elaborated in the system at that particular time.

When the phenolsulphonephthalein test is within the normal limit there, still may be renal deficiency, and the data obtainable by blood chemistry may not be in keeping with the apparently normal findings.

When the phenolsulphonephthalein test is below normal the questions arise: Is this a temporary phenomenon; is the phenolsulphonephthalein held in the tissues; will it not be higher if an intravenous injection be given; and can it not be improved by an operative procedure or by drainage? Even if evidences of retention of nitrogenous products are at hand in the blood values, we cannot be completely satisfied with the

[1] Chabanier and Galhardo, Séance et Mémoires de la Societé de Biologie, 83, 1920, p. 723.

findings unless we have recourse either to the Ambard coefficient or the concentration or accommodative tests.

With a very small phenolsulphonephthalein output of zero, up to 10 or 15 per cent., we always advise the associated employment of blood chemistry and either the Ambard or the accommodative test. With a zero phenolsulphonephthalein and high blood values we are in a dangerous zone. But it is only when, in addition, the Ambard coefficient is high, or the concentrating power is lost, and the tests for accommodative activity are defective, that we must consider the case inoperable.

The blood chemistry, too, when taken alone has its shortcomings. When the blood chemistry is repeatedly normal, a sense of security, it is true, is given us, but it may be normal in the presence of a minimal output of phenolsulphonephthalein, and when this is the case, we should not be content unless the Ambard coefficient or concentrative power gives us further guarantee. On the other hand, when urea, total nitrogen, creatinin, and uric acid are very high, we have positive evidence of renal inadequacy. It is in those zones where retention is moderate that we are again at a loss and must call to our aid the other methods. A very high uric acid content and high creatinin values are always suggestive of the existence of a chronic nephritis upon which a surgical lesion may be engrafted, or suggestive of an acute nephritis that supersedes the surgical lesion. Such high figures are usually of great moment, although patients may survive for months or more than a year with creatinin and uric acid values that are conceded by many of the modern school as being of fatal prognostic significance.

In short, none of the tests can be accepted at their face value unless checked up and confirmed with other of the important procedures. We recommend in urologic surgery the following: First, phenolsulphonephthalein for a rapid comprehension both as to the combined total function of both kidneys, and in rapid differentiation between the two kidneys and in the recognition of the diseased kidney; second, the blood values in the diagnosis of chronic nephritis for estimation of severity of

prognosis, and for the determination of the retention of waste products; third, the Ambard coefficient or MacLean index as a valuable adjuvant supplementing both the phenolsulphonephthalein test and the blood chemistry; and finally, one of the *two-hour tests*, that is, tests for the accommodative or concentrating power of the kidneys, either the Schlayer-Hedinger, the *two-hour renal test*, and the Mosenthal modification of the Strauss tests.

In most instances where the blood chemistry is repeatedly normal, the phenolsulphonephthalein test normal, and evidences of nephritis are absent, the urea being adequate and the specific gravity normal or near normal, a nephrectomy may be done without recourse to the other tests mentioned. But where we are dealing with bilateral renal disease, whether both kidneys are the seat of surgical lesions or whether the supposedly healthy organ is the seat of an antecedent chronic nephritis, the haphazard acceptance of an occasional phenolsulphonephthalein test, and an occasional estimate of urea nitrogen, total nitrogen, creatinin, and uric acid may not suffice and may be misleading. It is true that the experienced urologist may frequently dispense with the more complicated methods, but those with more limited experience should have recourse to that guarantee which the additional application of the Ambard coefficient or the MacLean index, supplemented with tests for concentrative power and accommodative response, may afford.

CLINIC OF DR. HAROLD E. B. PARDEE

NEW YORK HOSPITAL

MANAGEMENT OF PATIENTS WITH HEART DISEASE DURING PREGNANCY AND LABOR

I SHALL first show you 2 patients and then discuss with you some of the general principles which are illustrated by their condition.

The first, a woman twenty-seven years of age, had never had rheumatic fever, but had frequent sore throats when a child. She had never complained of palpitation or shortness of breath on exertion. One child three years ago born without unusual circumstances. This, her second pregnancy, was uneventful until the fifth or sixth month, when she began to be troubled by weak spells accompanied by a giddy feeling, and became somewhat short of breath on walking and on climbing stairs. Later she felt short of breath when lying flat in bed, and now, the eighth month, she can climb only one flight of stairs without resting and has to sleep with her head raised on two pillows.

Examination does not discover any dyspnea when standing at rest or when lying on her back without pillows. There is no cyanosis or edema of the extremities. The heart is slightly enlarged, the borders of dulness extending 3 cm. to the right and 10 cm. to the left of the midline, the left border being in the fifth interspace just lateral to the midclavicular line. The apex-beat gives a strong but sharp impact. The first sound at the apex is loud and sharp and there is heard there a short rough presystolic crescendo murmur and a long, loud diastolic rumble. No systolic murmur heard. The pulmonic second sound is accentuated and sharp and much louder than the aortic second.

The blood-pressure is 110/75. The lungs are negative for dulness, though there are a few fine râles at the bases posteriorly, which clear up after two or three inspirations. The Wassermann reaction is negative. The abdomen is very prominent and, an important feature in respect to her dyspnea, the diaphragm is evidently crowded upward by the uterine mass, which is large.

The diagnosis is plain enough, a mitral stenosis of occult, probably "rheumatic," origin. It is evidently a long-standing condition, and to judge by the loudness of the murmurs and the presence of enlargement of the heart is a definite stenosis of no mean degree. Of what character though should we consider her compensation? Is her cardiac reserve considerable or slight?

To determine this we will direct her to swing a 5-pound dumbbell twenty-five times from near the floor to high over her head at such a rate that it will take about fifty seconds. Now observe her carefully while respirations and heart-rate are being counted. You see she shows a moderate degree of objective dyspnea, and at first a slight appearance of distress in her facial expression, but both this and the dyspnea quickly disappear well before the end of the first minute after exercise.

The respiratory rate was 15 during the first half-minute and the heart-beat for the first ten seconds was at the rate of 126 per minute, slowing to 84 after one minute and to 72 after two minutes. Such a reaction would be classified as neither good nor poor, but as fair. So then, considering this reaction to exercise in conjunction with her history of freedom from symptoms on exertion until the middle of the present pregnancy and that the symptoms at present are not severe, I would say that this woman's compensation was fair. Her cardiac reserve is somewhat impaired, but certainly not seriously.

The second patient also has mitral stenosis. She is twenty-seven years of age and has had two previous labors, one four years ago and one eighteen months ago. Between these there was an early miscarriage. Her previous illnesses did not include chorea or rheumatic fever or frequent sore throats or colds. She first knew of her heart trouble at the time of the last pregnancy,

when the doctor told her of it. She had not been troubled by shortness of breath or palpitation and had not suspected any trouble with her heart. She was probably at this time in just about the same stage of her disease as is the first patient now, and if her exercise reaction had been tested at that time it would probably have been but little abnormal.

About six months after this pregnancy, a year ago, she began to notice that she was somewhat short of breath on walking fast and on stair climbing, and a few times she coughed up some bloody sputum. Six months ago she found that dyspnea was more easily produced, so that sometimes even walking at an ordinary rate would bring it on. At this time she had a cough which lasted for four or five months—during the winter and spring—and though the sputum was usually white, yet it was sometimes blood streaked. She did not feel sick, however, and went about her household duties as usual, avoiding heavy exertions which she found made her short of breath.

She was first seen at this clinic four months pregnant, and then complained of a slight cough. She was short of breath if she walked over a quarter of a mile at an ordinary pace, and much sooner if she hurried. She was unable to climb more than one flight of stairs without resting to recover from her dyspnea, and for two months had been able to do only the lightest housework.

On examination, she did not show dyspnea when standing quietly or when lying down on her back. She had the bluish-red color in the cheeks which is so common in patients with mitral stenosis, but the mucous membranes did not give the impression of being cyanotic and the nail-beds were a good pink color.

The heart was slightly enlarged, dulness extending 3 cm. to the right of the midline in the fourth space and 11 cm. to the left in the fifth space. The action was regular at the rate of 85 per minute. The apex-beat was sharp and strong, giving an impression of increased force. There was a plain, long, diastolic thrill felt at the apex. The first sound was sharp and loud. No systolic murmur, but a loud rough diastolic rumble with a

presystolic crescendo accentuation. The lungs were negative except for a few râles at both bases posteriorly, which did not disappear after several deep inspirations. The abdomen was negative except for the evidences of the four months' pregnancy. The legs were free from edema.

Here, as in the first case, was a long-standing mitral stenosis of considerable degree associated with some cardiac enlargement. The etiology was again occult, but probably "rheumatic." The compensation as suggested by the history of dyspnea on moderate exertion was not good, and the reaction to the test exercise was in agreement with this, for she showed marked dyspnea and considerable distress after twenty swings of a 5-pound dumbbell, the heart-rate going to 150 and the respiration to 36. The objective dyspnea continued for about two minutes and the heart rate fell to 120 after one minute and 102 after two minutes. This is a marked reaction and is due to a much reduced cardiac reserve.

The patient was evidently working very near to the limit of her heart's ability to carry on the circulation without being overtaxed. She was, therefore, directed to stop all housework, to avoid walking except when necessary, and to rest in bed for an hour in the morning and the afternoon. She was told to avoid eating large meals and to avoid drinking more than a moderate amount of fluid a day. Her tendency to constipation was to be combated by taking a tablespoonful of milk of magnesia at night or, if necessary, night and morning. She was given digitalis in full dosage, 20 minims four times daily for two days, three times daily for one day, and then morning and night, being told to continue this unless nausea or vomiting appeared. She was to return to the clinic on the seventh day. On the morning of this day she felt nauseated after her morning dose of digitalis. She was told not to take any more for three days, and to then continue with one dose each night unless nausea again occurred.

She did not return again to the clinic in spite of two visits by a nurse until two days ago, which was after an interval of three and a half months. She had been very well at first and had considered returning for treatment unnecessary, as she had

only minimal symptoms. She felt as well as she did before pregnancy, and so gave up the restrictions which had been imposed on her, and gradually did more and more walking and work about the house. During the last six or seven weeks she had noticed increasingly frequent dyspnea and palpitation on exertion, and for the last week could not lie flat in bed on account of dyspnea, having to sleep on three pillows and coughing frequently, raising bloody sputum. On admission she had a temperature of 99.6° F. by mouth, pulse-rate 120, respirations 24 per minute.

She was then much as you see her now, not dyspneic when at rest, but such exertions as moving about in bed would readily produce dyspnea. She has rather a loose cough, which raises a moderate amount of bloody sputum. The mucous membranes are perhaps a little cyanotic. She must lie upon a bed-rest to be comfortable, as lying down flat makes her feel that she is suffocating. The heart is as on the previous observation, except that the left border is about 1.5 cm. further to the left of the midline, a result possibly of lateral displacement of the apex due to the diaphragm being raised by the uterine mass. There is, however, an abnormal filling of the veins of the neck and arms which was not present before, and the lungs have râles at the bases posteriorly on both sides as high as the angle of the scapula. The uterus is rather small than large, and seems to be somewhat within the pelvic brim. There is a minimal edema of the legs below the knees. This, of course, need not be due to cardiac failure, but to the pressure of the uterus upon the venous and lymphatic channels of the legs, as it is seen in a fair number of pregnant women who have normal hearts.

Both of these women have loud, well-developed murmurs of mitral stenosis, and both have some cardiac enlargement, so that they both, from the viewpoint of pathology, belong to a type of heart disease we have been told to fear during pregnancy. A statistical study of our cases, however, does not bear out such a teaching. We find among the serious cases a large percentage of mitral stenosis, but no larger than the great frequency of this lesion should warrant. In a group including all

patients whose cardiac condition necessitated special treatment during pregnancy or labor we did not find the percentage frequency of mitral stenosis any greater than in the group of patients whose cardiac condition was not a source of concern. We did find a complete absence from the more severe group of patients whose only valvular lesion was mitral regurgitation, and a considerably greater frequency in this group of patients with both mitral stenosis and aortic regurgitation, though there were some of these latter in the mild group.

It seems very evident that neither the murmurs nor the valvular lesion can be used as an indication of the severity of the patient's condition at the time, or of the likelihood of an uneventful progress. There was no evident difference between the pathology of the 2 cases I have shown you, and yet there was a great difference in their physiology. It is on the observable features of the patient's physiology that we must make our decision as to the treatment and as to the prognosis. It would be very desirable if these features could be summed up and expressed by a single test of cardiac function, but it does not seem at the present time that there is any test which does this with accuracy. It is necessary, therefore, for us to consider many features of the case. The history gives the patient's idea of the limitation of her ability. The physical examination tells us how marked the cardiac disease may be, allowing us to deduce the severity of the heart's handicap. Besides these we must give the patient a rather strenuous test exercise to perform and observe her reaction to this, so that we may be able to check up objectively her statement as to the degree of her limitations. Combining these three different methods of attacking the problem we should be able to gain reasonably accurate impressions as to the condition of the patient's circulation—whether it is at present normal or subnormal, and if normal, how much reserve is available for increased effort.

Now let us consider for the moment the strains that pregnancy imposes upon the heart. During the early months there is a slowly increasing body weight which means both anabolic activity for tissue building and increased physical exertion to

carry the increased weight. Both of these demand an increased transportation of oxygen and, therefore, either increased blood volume or an increased rate of flow. The capillary bed increases in area also, so that there is no doubt that the heart has to constantly use some of its reserve force during pregnancy. This is evident in the increasing limitation of the ability to exercise without causing dyspnea and rapid heart action which any normal woman will observe at this time.

These strains continue, and at some time about the fifth month there is an added factor in the shape of a crowding upward of the diaphragm by the uterus. This does not affect the heart action directly, but does limit the expansion of the lungs. The same amount of increase in pulmonary ventilation now causes more muscular effort on the part of the patient, so that the heart must now maintain a proper aëration of the blood by increasing its output per minute; where otherwise the aëration would have been increased by an augmented pulmonary ventilation. This is a very definite strain upon the heart, but there is such great variation in the degree of crowding of the diaphragm in different women that this factor will be one of the great individual variables which favor some women and work against others.

Then there is the personal element—the extent of the patient's activities—whether she goes about a great deal or remains quietly at home. Whether she has servants in her house or whether she does housework and cares for 2 or 3 children, whether she is of an excitable temperament or phlegmatic. All of these things have an influence upon the demands which are going to be made upon the heart, and so upon its ability to last through without being overtaxed.

Last of all is the labor itself. A precipitate delivery causes the minimal strain upon the cardiac reserve, and probably a very slight one. On the other hand, a long, difficult labor with prolonged straining and effort constitutes a physical exertion which is comparable with many athletic events, and is much more prolonged than most, so that such a labor is a severe tax upon the heart's reserve power. The severity of a labor is no-

toriously a difficult thing to predict. The size of the bony pelvis, the size of the child, the distensibility of the soft parts, the expulsive force of the muscles, are each difficult to estimate, and a slight error in our conception of one or two of them might make all the difference between an easy labor and a difficult one.

Thus there is as much variation in the amount of strain to which the heart will be subjected in different individual patients as there is in the ability of their different hearts to withstand strain. In each decision as to management we must take into account not only the heart disease and the heart's physiologic ability, but an estimation of the amount of strain that pregnancy and labor are likely to cause in the particular patient.

Now as to the application of these principles to our 2 cases. The first woman, you will remember, had a well-developed mitral stenosis, with some enlargement of the heart. She did not show evidences of cardiac insufficiency before pregnancy and only slight symptoms after its beginning until the seventh or eighth month. The uterine mass was large and high in this case, and undoubtedly contributed a definite share to her discomfort. Her reaction to the test exercise was fairly good. She was not a primipara and her measurements and muscular development did not seem to offer any reason why her labor should be difficult. We need not be concerned about the outcome in her case, but nevertheless it is always advisable to record the pulse and respirations every half-hour during labor, so that we may receive warning of the onset of cardiac failure in time to act before it is severe. If the pulse-rate stays below 90 per minute and the respiration below 25 there will be no cause for alarm, but if the pulse goes to over 100 or the respirations to 30 per minute, it should be taken to indicate that the heart is being overstrained.

As soon as this condition is appreciated we should endeavor to bring the labor to a prompt ending unless it should appear to be promptly ending itself. A continuation of the overstrain will lead to more and more severe cardiac failure, and the end-point will be that very undesirable condition—edema of the lungs. If a low forceps application can be done it should be promptly resorted to. If it cannot, then a choice between high forceps

version and abdominal section must be made. The last of these seems to me to be by far the safest, for it gives quicker relief from labor than the others and does not itself impose as much added strain as they. Patients with cardiac disease take ether very well, and especially if anesthesia is started with a little chloroform, so that the initial stage of excitement and possible struggling is reduced to a minimum. I consider gas very inadvisable for these patients, but I am not so certain about gas with oxygen, as I have not seen it used in cardiac disease. It is hard to see how the chloroform-ether combination could be improved upon however.

The first of our patients does not seem to be a case which will need any form of interference because of her cardiac condition, for her cardiac reserve seems to be but little reduced. She should be well able to stand the strains of labor. Not so with the second patient. If labor were to start in at present she would be in a very precarious position, for without it she shows marked evidences of cardiac failure. The likelihood of avoiding intervention in her case lies in the fact that her condition may be improved before labor sets in, to a degree of compensation that will allow her to go through it without the heart being overtaxed. Proper rest and treatment were able to improve her greatly in the early months of pregnancy, and so it seems likely that they will be able to do the same now. This is especially likely because her history shows that of late she has been continually attempting to do things which gave rise to discomfort, that is, continually pushing her heart beyond its ability. When this continued overstrain is stopped the heart will recuperate, but the extent of the recuperation can only be found out by trial.

Certainly immediate interference is contraindicated. The heart is showing signs of failure and we should not impose the added strain of operation at this time. It is a safer policy to first try medical treatment and by this means to get the heart in as good condition as possible. Should two weeks of medical treatment fail to improve the circulatory condition, or even should this show signs of growing worse during the first week of

treatment, we must then operate. Failure to improve under treatment makes it evident that something must be done, and so whatever extra risk is incurred by operation must be incurred.

Here again we meet the question of what operation shall be chosen, and here again I favor abdominal section on the grounds that it is the quickest and imposes the least strain on the mother's heart. An induced labor is apt to be prolonged and may eventually necessitate an anesthetic also.

The second patient, then, should be put to bed. If she cannot lie down with comfort she may use a back-rest. Her diet need not exclude any special class of food, but should be a low diet, and especially low in liquids, not taking over 30 ounces of liquid in the twenty-four hours. She should also receive digitalis, 30 minims of the tincture in 2 ounces of water, three times daily for three days (for only two days if she weighed less than 120 pounds), and then twice daily, morning and night, unless nausea, marked depression, vomiting, or pulse irregularity appeared to indicate poisoning with digitalis, or a marked slowing of the heart-rate to indicate definite therapeutic action. If signs of poisoning appear we should stop the drug until they disappear and for forty-eight hours more, and then resume with a daily dose of 20 minims of the tincture taken at night. When therapeutic slowing of the heart appears before the signs of poisoning we should immediately reduce the dose to 20 minims a day, so as to prevent the cumulative effect of larger doses.

Under this régime we shall expect to see signs of digitalis effect on the third, fourth, or fifty day, and by the end of a week the patient should have begun to feel better and to breathe easier. Another week or ten days in bed on the same régime and we shall gradually allow her up in a chair, starting with a half-hour a day, and increasing to one hour, two hours, three hours, and so on, until she is up for most of the day, provided that this process of allowing up does not cause a maintained rapid pulse-rate, as noted at the usual four-hour intervals. When she has sat up for three hours without fatigue she might begin to walk a few steps, and gradually increase these as she finds she is able, without bringing on palpitation or dyspnea.

If all goes as I should expect this woman will come to be up and about again, and then the problem will present itself as to what should be done in regard to continuing her pregnancy. She will now be able to stand an operation without much danger, so we must now advise her whether she can proceed to full term or whether interference is indicated. For making this decision the remote, extracardiac factors are of the utmost importance. If it is possible to make her life easy from the present time until two or three months after labor, if she can be relieved of the necessity of doing housework and of a part of the care of her child after it is born, then I would be much more inclined to allow her to go on to labor than were she already the mother of 2 or 3 children and compelled to take care of them and to do her housework besides. Such surroundings would be very liable to lead to another decompensation before labor, or to make her compensation more precarious at the time of labor, or to make her postpartum recovery slow and uncertain. A woman who has had a period of decompensation during or shortly before pregnancy should be under the most favorable circumstances if her pregnancy is to proceed. Otherwise we are taking an unjustifiable chance with her health and perhaps with her life. On the other hand, if there are special family reasons why a child is very much wanted it should be possible in almost every instance to carry the woman successfully through to the time when a viable child can be obtained.

When labor sets in in such a case careful observation of the pulse and respiratory rates will keep us informed of the reaction of the heart to the strain of labor, and, as was said when discussing the first patient, the prompt interruption of labor when the pulse or respiration are persistently above 100 or 25 respectively, will save the heart from the danger of overstrain with its resulting acute cardiac failure.

I feel that before closing I should say a word about the treatment of the acute cardiac failure that is seen during pregnancy. It may appear at any time after the third month in response to a severe exertion. I have seen it twice following sexual intercourse after the fifth month, once following the

administration of nitrous oxid while incising a small carbuncle, once following a violent altercation with the husband, several times during and immediately after labor, and twice it has appeared without any apparent cause about an hour after delivery. The condition of the patient is one of marked prostration, with marked shortness of breath, orthopnea, cyanosis, congestion of the peripheral veins, and the coughing up of bloody frothy sputum. An edema of the lungs is present with many moist and bubbling râles, while the heart is rapid, the sounds faint, and the pulse small and weak, usually regular.

These patients should be placed absolutely at rest. Moving them to a hospital may be the cause of a prompt death because of the extra strain on a heart already severely overtaxed. Above all, there should be no operative procedure. Absolute rest in bed with a back-rest to facilitate breathing, and the hypodermic administration of ¼ gr. of morphin sulphate along with 1/50 gr. of atropin sulphate, are the immediate indications. Also, if the neck veins are evidently much distended with blood, a phlebotomy should be done, and continued until this overdistention of the veins is abolished. The distention is a sign of too high a pressure in the superior vena cava and right auricle, and though the result of failure of the right ventricle, it likewise is a handicap to the ventricle because of the overfilling at each diastole.

It is advisable, too, to give some preparation of digitalis intravenously for its stimulation of the heart muscle. My preference is for digitoxin, which can be given in a single dose equivalent to 0.01 mgm. per pound of body weight of the patient, *e. g.*, 1.5 mgm. for 150 pounds. If necessary, another dose of half this size, *e. g.*, 0.005 mgm. per pound, can be given six hours later, and at this time the oral administration may be started, giving a 30-minim dose of the tincture, repeating this if needed, and if signs of digitalis action do not appear at intervals of six hours.

If the patient still appears to be very cyanotic after the phlebotomy, oxygen inhalations should be administered from a closed system similar to the Bennett inhaler, allowing rebreath-

ing into the bag containing oxygen. The classic method of administering oxygen by a funnel attached to a tube from the tank has been shown to be of very little value in increasing the concentration of oxygen inhaled. Lacking a closed inhaler the tube from the tank may be allowed to discharge into the air about an inch from the mouth or nostril of the patient so that the stream of oxygen is forced in with the inspired air. This is better than the "funnel method," but not so good as rebreathing oxygen from a bag. Whichever method is used, the oxygen should be inhaled for at least fifteen or twenty minutes before deciding that it will not help the cyanosis. The edema of the lungs makes it difficult to get the oxygen in contact with the alveolar capillaries, and it is only there that it can be absorbed into the blood. In some cases one period of inhalation is sufficient, while in others it may need to be given for fifteen minutes every half-hour.

When edema of the lungs sets in before labor the chances of recovery with this treatment are good. We have seen but one death under these circumstances. When edema sets in during labor the chances are not so good, and depend largely upon how far the labor has progressed. I feel confident that with proper watching of the pulse and respiration and the bases of the lungs during labor, and with prompt intervention when the signs of danger make their appearance, there will be few if any of these serious occasions during labor. If you should see one after it has set in, however, do not rush the patient to operation. Absolute rest is the first indication, and this must include the checking of the labor by morphin; 1/50 gr. of atropin sulphate should be given with this. Phlebotomy is indicated if the neck veins are greatly distended, and digitoxin and oxygen should be used as previously described, but do not push the oxygen if it annoys the patient and prevents her resting. This treatment will improve the circulation in the majority of cases, and when labor again sets in with vigor interference will be safer than before treatment. The operation should be the one involving the least manipulation of the mother and yet should end the labor promptly. The statement that it should be either a low or

medium forceps or an abdominal section will need few exceptions, and there should be little fear of ether anesthesia, as it is very well tolerated by patients with cardiac failure, but should, as has been said, be started with a little chloroform to avoid the possible struggling during early etherization.

CLINIC OF DR. CONNIE M. GUION

NEW YORK INFIRMARY FOR WOMEN AND CHILDREN

A TYPICAL CASE OF PERNICIOUS ANEMIA

THIS patient presents a classical picture of pernicious anemia. He was observed over so long a period and showed so many of the vicissitudes of the disease that it seems worth while to cite his history.

He was fifty-five years of age when he first came under the observation of Dr. Frank S. Meara[1] and the late Theodore Janeway in 1913, and the diagnosis of pernicious anemia made.

The previous history revealed the fact that the diagnosis possibly could have been made in 1906 had a careful examination of his blood been made and his symptoms properly interpreted. At that time he consulted a doctor for "stomach trouble" and a stomach analysis revealed an achlorhydria. But a more important point is that he had a *sore* and *swollen tongue*. I want to lay emphasis on this finding—a sore tongue is frequently the earliest symptom of pernicious anemia, and it is too often dismissed as a symptom of indigestion without due consideration of its possible grave significance.

In 1908 the patient was unable to distinguish colors, everything looked white to him; he could recognize no one by sight, he could not read. The oculist made a diagnosis of toxic tobacco amblyopia at first, but later retracted the diagnosis. In view of his later history it seems probable that this was a toxic amblyopia due to pernicious anemia.

In 1908 to 1913 the man suffered almost constantly from bleeding piles. Three times he was operated on, but never with real relief, so that he lost considerable blood over protracted

[1] I am indebted to Dr. Frank S. Meara for the use of this patient's history from 1913 to 1919.

periods. From 1913 until his death in 1920 he continued to bleed, but the volume of blood was less than before this date.

In 1913 he was complaining chiefly of general weakness and inability to stand without faintness. His memory was poor and he was very irritable.

The physical examination at this time showed a well-developed and well-nourished man of a marked pallor, but not in the least of a lemon tint. The lips and scleræ were pale, his tongue was pale, but not ulcerated or atrophied. Hemorrhages were not noted on the skin or on the mucous membrane. There were no enlarged lymph-nodes. The cardiac outline was not increased; a soft systolic murmur was heard at the apex and at the base of the heart. The blood-pressure registered 106 in systole and 95 in diastole. Edema of the legs and ankles was slight. The liver and spleen were not palpable.

The late Dr. Theodore Janeway, on the basis of these findings, made a diagnosis of chronic hemorrhagic anemia as the most likely, and pernicious anemia as the next possibility. The blood-count was to be the deciding factor.

Dr. Frank S. Meara, who also saw him at this time, diagnosed the condition as being most probably pernicious anemia.

A blood-count done in Dr. Janeway's office showed: Polymorphonuclears, 38 per cent.; lymphocytes, 53 per cent.; eosinophils, 5½ per cent.; basophils, ½ per cent.; myelocytes, 2½ per cent. The red blood-cells were deeply stained. They showed marked anisocytosis, marked poikilocytosis, some polychromatophilia, a number of macrocytes, 10 megaloblasts, and 7 normoblasts in 200 cells counted.

The hemoglobin was 37 per cent. and the total red blood-cell count was 1,600,000, with a color index therefore of 1+.

On this count Dr. Janeway made a diagnosis of pernicious anemia and gave a prognosis for life of two months.

The treatment consisted of rest in bed and Fowler's solution by mouth or sodium cacodylate hypodermically. Within one month the blood-picture had risen to 85 per cent. hemoglobin and 3,600,000 red cells. He then left the city and took his medication by mouth only. Within a month the hemoglobin dropped

to 65 per cent. and the cells to 1,960,000. Sodium cacodylate hypodermically was given daily for two weeks, at the end of which time his hemoglobin rose to 75 per cent. and the cells to 3,840,000.

During the next six months the man felt fairly well, and a report of his blood by Dr. Janeway showed a pretty normal picture except for anisocytosis. Two weeks out of every month he received arsenic and during the period of medication his blood-picture usually improved.

At the end of about ten months after he was first seen he started on another crisis, and within two months his blood was the same as Dr. Janeway had described it just a year previously. The physical examination was practically the same except that his skin was now lemon yellow and the gait unsteady.

This time it took him two and a half months to build up his blood-count to the point that it attained in one month before. After six months he felt so well that he discarded arsenic and doctors.

For eighteen months he enjoyed a remission and then he noticed that he was tiring again more easily, he had no inclination to work, his lips were dry, his tongue and mouth were sore for the second time in ten years; he had an annoying flatulency and anorexia. His eyesight was weak again, and he now had a sternal pain from which he was rarely free up to his death. He was smoking excessively. An examination showed absent knee-jerks, enlarged liver and spleen, bleeding hemorrhoids in addition to the former findings. This was now three years after the diagnosis was first made.

Compare the man's subjective symptoms of profound prostration and the new neurologic findings with the blood-picture, and note the curious dissociation between the effect of the toxins of the disease on the nervous system and the hematopoietic system. His blood-count was at this time: Hemoglobin, 85 per cent.; red blood-cells, 2,740,000; color index, 1.6 per cent.; leukopenia.

The blood-smear showed no pathologic red blood-cells according to the report.

The Wassermann was negative for a second time.

He received daily hypodermics of sodium cacodylate. After a week his knee-jerks had returned, though they were obtainable only by reinforcement; later they were normal.

For a month the blood became progressively more pathologic, with a corresponding change in his symptoms. Then the blood-curve started upward and improved continuously for two months. In the meantime he felt and looked worse every day. His tongue became broad and fissured. He had a swaying sensation, and numbness in the lower extremities.

Arsenic was given him as on the other occasions, but his blood-cells and hemoglobin continued to decrease and his symptoms never abated. After nine months the late Dr. Edward Lindeman transfused him with 1480 c.c. of whole blood. The improvement in the blood reached its peak in one week; the hemoglobin rose from 30 to 55 per cent. and the red cells from 1,230,000 to 2,990,000. At the end of eight weeks his blood-picture had reached the same level as before the transfusion. Dr. Lindeman repeated the operation with the same result, *i. e.*, a rise in hemoglobin and red cells for about one week followed by a constant drop for the succeeding eight weeks. At this juncture Dr. Frank Meara advised him to submit to a third transfusion and to consider the advisability of a splenectomy. While he was debating the question he had a sudden remission. In four weeks his hemoglobin had jumped from 36 to 50 per cent. and the red cells from 1,880,000 to 2,316,000, but he continued to run a leukopenia of 2600, with 30 per cent. polymorphonuclears.

At the end of this remission he had two teeth with root abscesses extracted, and, of course, we do not know what part this played in his improvement.

During the next two months he had no medication and his physical condition and blood-picture improved more markedly than at any previous time. For five months he enjoyed a feeling of well-being that he had not known for five years.

It is such natural remissions as this that make us wonder whether our treatment has any real effect.

The end of this remission was marked by the return of all

the old nervous manifestations—drowsiness, numbness and tingling of the hands and feet, toes feeling dead, pain in the sternum and spine. The blood-count showed a striking contrast to the neurologic symptoms, for it was better than it had been in two years, while he felt worse than at any time before. Two weeks after the onset of this remission the blood-count started to fall and continued to go down steadily. The cord symptoms, on the other hand, did not progress, but, on the contrary, they were in complete abeyance at times, so that we could see no correlation between his blood findings and subjective symptoms.

For six months he was on the down grade. He refused to be transfused until his condition was so desperate that a fatal issue seemed imminent. He was emotional, irritable, and exhausted. He would faint on assuming an upright posture and at stool. He had a marked myocardial let down—the heart sounds were poor, the pulse was 120 and weak, his legs were edematous, and the blood-pressure was 98 in systole and 50 in diastole. The hemoglobin was between 25 to 30 per cent., the red cells 1,720,000, and the white cells 1370 on repeated counts.

Dr. R. E. Stetson transfused him with 1230 c.c. of blood. After the transfusion he had a slight reaction, but he no longer felt so weak and faint. The neurologic symptoms varied. The blood-count after a week dropped steadily, so that at the end of three weeks we decided to transfuse him again before he could lose the benefit of any stimulation from the former one. Dr. Stetson repeated the transfusion, using about the same volume of blood from a different donor. The patient had no untoward reaction from the transfusion. Three days subsequent to the transfusion a blood-smear showed polychromatophilic cells which indicated that the bone-marrow was being stimulated. But at the same time the hemoglobin and number of red cells were decreasing progressively. They reached their lowest level at the termination of three weeks, and then the picture began to improve until it attained its maximum in three months—hemoglobin, 92 per cent.; red cells, 4,500,000, and the blood-smear normal.

In the meantime what was the clinical course of the dis-

ease? Daily the man complained of pain under the sternum, in the spine, especially in the cervical and lumbar regions. He felt as if he were sitting on a ring air-cushion, as if he had a belt around the waist. He had pricking sensations in his hands and arms and the muscles of his arms and legs twitched so that he would be awakened out of a sound sleep. He had never been so irritable and nervous.

His knee- and ankle-jerks were absent, the abdominal reflexes were intact. A Babinski, ankle-clonus, and Romberg were definitely positive. He could walk only with the help of two assistants.

Reëducational exercises to overcome the static and motor ataxia were practised daily. After five weeks he could walk fairly well, but he had a tabetic gait. In eight weeks he walked a mile. The Babinski and ankle-clonus had disappeared, but Romberg's sign and absent knee-jerks persisted. For a month the cord symptoms cleared up, but only to return with greater intensity. In addition to the old discomforts he had a sensation of sweating (when his skin was dry) that would awaken him at night. He complained also of a disturbance of vision. In his own words, "It is as if a swarm of gnats are in front of my eyes, my vision is hazy, there is a sensation of shimmer or flicker like heat waves." These were new symptoms and besides them he had all the old ones of ten years ago, *i. e.*, an inability to see at a distance, no color sense, everything was white. These sensations came on in periods and were worse in the sunlight. He consulted Dr. John E. Weeks about his eye condition, and was advised to discontinue smoking. After six weeks' abstinence from tobacco the eye condition was not improved. Dr. Weeks reported that the disturbance might be a toxic tobacco reaction, but that it was more probably a manifestation of the anemia.

About a month later his hemoglobin and red cells had begun to fall off a few points and we were giving him hypodermics of sodium cacodylate. The morning before he died he was in the office. He said that he was "feeling great" except for the limitation in his vision; he had slight tingling in his hands and feet and some substernal pain. His gait was suggestive of a tabetic,

but he could walk several miles without fatigue. The Romberg was entirely absent. He had no knee-kicks or ankle-jerks. His blood-count was: Red blood-cells, 3,900,000; hemoglobin, 80 per cent.; white cells, 9500; polymorphonuclears, 75 per cent.; lymphocytes, 16 per cent.; mononuclears, 3 per cent.; eosinophils, 2.5 per cent.; basophils, ½ per cent. The red cells showed polychromatophilia and anisocytosis.

When he retired that night he was in excellent spirits. About 2 A. M. his wife was awakened by his moaning. She found him collapsed in the bed, his face was cyanotic and he was breathing in gasps, and died before a doctor saw him. No autopsy was performed and the cause of the death is unknown. However, the age of the man and the character of the substernal pain from which he so often suffered suggest the presence of a sclerosis of the coronary arteries and that the cause of his death, occurring when his anemia was not marked, was a coronary thrombosis.

In reviewing this case we are impressed by the character of the early symptomatology. Beginning fourteen years prior to his demise he complained of general weakness, stomach trouble, a sore tongue, and bleeding hemorrhoids; the laboratory examination of the gastric juice at this time revealed an anacidity. When we follow the course of the disease the persistent recurrence of these symptoms is striking. After ten years the first neurologic symptoms and signs appeared, he had absent knee-kicks and tabetic gait, numbness and tingling in the hands and feet. From this date it was the nervous disturbances that were most annoying and disheartening to the patient because they were so oddly dissociated from the blood-picture. At times when the hemoglobin was rising constantly the central nervous system seemed most affected by the toxins of the disease.

When we consider the efficacy of the treatments instituted we realize that while a remission would follow upon some measure instituted on one occasion, at another time the same procedure affected absolutely no change. Again, a spontaneous improvement would occur absolutely dissociated from any treatment whatsoever. Further, in analyzing the remissions, we know that at no time was the man well; at no time did he have anything

more than a temporary abatement of either one or the other group of symptoms, and the neurologic ones always seemed most persistent.

To follow this man's case and recall how often a fatal issue seemed inevitable, and how many times he rallied and returned to active business, gives us an insight into the difficulty of making any kind of prognosis for life. When so eminent a clinician as the late Theodore C. Janeway gives a man a margin of life of two months, and he takes seven years, it behooves the rest of us to be guarded in our pronouncements.

This case illustrates admirably most of the symptoms of pernicious anemia and presents them in the order in which they often occur. However, it is imperative to remember that the initial symptomatology is very variable and that it is the *early* symptoms and signs that we must be on the alert to recognize. Furthermore, it is important to keep in mind constantly the fact that the symptom-complex of pernicious anemia is not developed in direct proportion to the change in the blood-picture, as I have pointed out in the case reviewed above.

The patient may present himself complaining of general weakness, a disinclination to work, of palpitation of the heart, dyspnea, vertigo, and edema of the legs. If a careful blood-count is done we may find a well-marked primary anemia or a normal picture.

Or this patient may have but one symptom—a sore tongue; a tongue that feels raw; a tongue that will burn when he eats acids, spicy or hot foods. At times it is fissured and ulcerated on the sides and tips, and later the papillæ atrophy until the tongue looks smooth and small. At first these symptoms come and go and the patient forgets that he ever had them, but eventually they become more annoying and the periods of remission are shorter. The tongue may be very painful when the blood-picture is at its best. By careful questioning this early symptom can be elicited in a large number of cases. Finally, there are other gastric symptoms which are laid often to the sore tongue: the patient is afraid to eat at first because of pain in his tongue, then he has an anorexia, nausea, gas, heart-burn. Food

may become repulsive to him. He may have diarrhea and lose weight. If a gastric analysis is done on the patient with such complaints it will show in a large percentage of cases an *anacidity*. Again, the patient's only complaint may be "stomach trouble" —consisting of heart-burn, gas, anorexia, and anacidity. The blood must be examined, for it will usually give the solution of the diagnosis. If a first count is normal we should repeat it at frequent intervals until some explanation can be found for the gastric pathology.

Finally, the earliest symptom that annoys the patient may be referred to the central nervous system, *i. e.*, a tingling and numbness in his hands and feet. They may be so disturbing that he cannot concentrate on his work. The area affected by these sensations may extend so that the entire arms and legs are involved. He may suffer from these disturbances for several years before he has any other complaint. Then he may have either cardiac or gastro-intestinal symptoms or further involvement of the central nervous system. He may develop a muscular weakness so that his knees are weak, he stumbles when he walks in the dark, he loses his balance easily. He may have a sense of constriction about the waist, difficulty in urination and defecation, and all the other classical signs of a tabes dorsalis (posterior sclerosis). On the other hand, the symptoms may be those of a spastic paraplegia (lateral sclerosis): a gradually increasing stiffness of the muscles of the legs, cramps and twitching in the leg muscles, increased reflexes, a positive Babinski; a brisk clonus of the knee and ankle. Or the picture may be a combination of a posterior and lateral sclerosis. The Wassermann in such cases is usually negative and there is no history of syphilis. The spinal fluid is not characteristic.

Nervous symptoms of some type are present in about 75 per cent. of all cases of pernicious anemia.

A blood-count, as emphasized before, may be normal or typical of the disease, and should be repeatedly taken, if normal, until the diagnosis of pernicious anemia can be excluded.

In short, the syndrome of pernicious anemia is a very variable one within narrow limits and it is not related always to the same

degree of change in the blood. It may simulate other common diseases, and if we are not on our guard and make routine blood-counts we shall often miss a diagnosis that could be made easily and will be made by someone else more painstaking. As a patient with this disease is studied over a prolonged course most of these symptoms may be observed, though they may appear at very different stages in different individuals and be related to very different degrees of changes in the blood-picture.

The physical examination of the patient which I have described gives a good picture of the disease.

We see a patient of a very pallid or of a greenish-yellow tint, but described often as that of a lemon, in apparently good nutrition in striking contrast to the emaciation in profound secondary anemia. The skin, mucous membranes, and retina may or may not show small hemorrhages. These should be looked for, especially between the fingers and toes, in the conjunctivæ, and on the soft palate. The tongue may be red and pale, ulcerated, fissured, and the papillæ atrophied, so that it looks strikingly smooth.

The heart is usually somewhat dilated, the sounds are fair, a systolic murmur is present, the pulse is rather rapid, and the blood-pressure varies according to the pressure of the individual concerned, but is not necessarily low even in a profound anemia.

The edge of the spleen is palpable in the average case and in 40 to 50 per cent. it is distinctly enlarged. The liver edge may or may not be felt, but it usually is palpable in well-developed cases.

The neurologic examination should be made with great minuteness, keeping in mind the fact that lesions are often patchy and give both motor and sensory disturbances—give the picture either of a tabes dorsalis or spastic paraplegia or of a combined posterior lateral sclerosis.

Among the most important signs to test are the patient's gait, the abdominal, arm and leg reflexes, presence of a clonus, Babinski, Romberg, dynamic ataxia (testing by running the heel along the tibia), static ataxia (tested by having the patient gage the position of his heel with relation to the bed), "bathyanes-

thesia" (a loss of deep sensibility so that the patient does not recognize in what direction his toes are moved, etc.), thermal reactions, paresthesia, and anesthesia.

Finally, the physical examination must include a thorough search for the presence of a new growth, especially in the abdomen, rectum, vagina and breasts, and prostate, and an examination made for hemorrhoids. These cases often run an irregular temperature as high as 101° F.

After a careful history has been taken and physical examination is complete we must resort to the help of the laboratory before we can make a final diagnosis. The blood-count is the first test to be made.

We can never make a positive diagnosis until the blood shows some of the characteristic changes of the disease.

The blood-picture may show:

1. A decrease in the total blood volume.

2. A marked diminution in the red blood-cells even to as low as 700,000 to 800,000.

3. A drop in the hemoglobin which is comparatively less than in the number of erythrocytes, so that the color-index is higher than one.

4. The change in the red blood-cells is one not only of number but also in the size and shape and staining qualities. Minot and Lee state that the deeply staining macrocytes along with the microcytes and large oval cells are the changes in the cytology most characteristic of pernicious anemia. Furthermore, the lack of achromia is a helpful differential point from secondary anemia where it is so marked early.

In examining the blood-smears one should keep malaria in mind and look for parasites. And recently pathologists have been paying more and more attention to the reticulated red cells.[1]

[1] The reticulated red cells may be demonstrated by this simple procedure:

1. Prepare a saturated solution of brilliant cresyl blue in 5 c.c. normal (0.85 per cent.) sodium chlorid solution. This solution must always be freshly prepared.

2. To 5 c.c. of normal (0.85 per cent.) sodium chlorid solution add 2 c.c. of sodium oxalate solution 2 per cent. Add 1 to 2. Shake thoroughly. Put

These are believed to be very early forms of red blood-cells. Minot and Lee say that they are the best single indication of activity in the red bone-marrow, so that they are important to determine not only for diagnosis, but for prognosis. The prognosis is best when they are increased in number and the size of the cells is normal rather than enlarged. The normal count is given as 0.5 to 2 per cent., with an average of 0.7 per cent. In pernicious anemia they may be 5 to 15 per cent., while in chronic hemolytic jaundice they are often 15 to 20 per cent.

5. The white blood-cells should be carefully studied. The number may be normal, but is usually reduced. It begins to change often earlier than the red blood-cells, rising during a remission and falling in the crisis. The same is true of the polymorphoneutrophils. Several observers have noted the increase in eosinophils in the blood of pernicious anemia. They may be as high as 10 to 15 per cent. Minot and Lee state that an increase in these cells is a good sign.

6. The platelets[1] undergo changes similar to the white blood-cells, but are believed to show less transitory variation than the polymorphonuclears because they are less influenced by physiologic reactions. A marked decrease in number and increase in size is characteristic of pernicious anemia. The normal count averages 250,000.

2 c.c. in a centrifuge tube. Prick the finger and add 5 or 6 drops of fresh blood directly to the stain. Shake well and let stand five minutes. Centrifuge. With a capillary pipet remove the sedimented cells and smear on a warmed glass slide as in an ordinary blood-smear. Let dry naturally. Study with an oil immersion (Vogel & McCurdy, Archives of Medicine, 1913, xiii, 707). The smear when properly made has a bluish-green tint and the cells show skeins or rods of darker staining bodies. The presence of nucleated red cells and megaloblasts is looked upon often as essential to our diagnosis. But this is far from the case. We may have a well-advanced case of pernicious anemia with never an erythroblast demonstrated. The presence is a good prognostic omen. Megaloblasts occur frequently with other abnormal cells. If they are present with small numbers of reticulated red cells the prognosis is poor, whereas it is good if the number of reticulates is high.

[1] These may be counted easily by using as a diluent a 2 per cent. solution of sodium oxalate in doing red blood-counts. The platelets are seen as highly refractile bodies much smaller than the red cells. The pipet should be shaken at least five minutes before the count is made.

7. The bleeding time varies with the number of platelets present. Hence it is usually increased, though not markedly, in pernicious anemia, where the platelets are low. The normal is about three minutes. If under ten minutes it is considered a slightly delayed reaction.

8. The coagulation time in a normal individual is five to ten minutes. In this disease it is delayed somewhat. In taking this it is important to use blood taken by venupuncture and not squeezed from the tissues.

9. The fragility test[1] is important for a differential diagnosis. In pernicious anemia the cells are often unchanged, but they may show an increased resistance.

Further laboratory tests must include careful observation of the feces for blood (after the patient has been three days on a meat-free diet), ova, and parasites, and an increased amount of urobilin which occurs when there is rapid blood destruction.

The urine may contain large quantities of urobilin under similar conditions. There may also be a hematuria or a hemoglobinuria. Albuminuria and casts are common.

A gastric analysis is of very important diagnostic value. Levine and Ladd in a series of 150 cases found an achlorhydria in 99 per cent. The anacidity may antedate the typical blood-picture by a number of years, as in the case cited above. Hence the necessity of doing repeated blood-counts on patients with "chronic indigestion" with absence of hydrochloric acid (Bulletin of Johns Hopkins Hospital, August, 1921).

We are now possessed of the factors that enable us to make a

[1] The determination of the resistance of the red blood-cells must be made accurately to have any significance. Weigh on a chemical balance 5 gm. of chemically pure sodium chlorid dried in the oven at 120° C. for an hour or more, and make up to 500 c.c. with distilled water in a volumetric flask. From this 1 per cent. solution prepare a series of dilutions so that strengths ranging from 0.3 to 0.6 per cent. are obtained, varying by intervals of 0.025 per cent. Keep in *tightly stoppered bottles*. With a red counting pipet draw up blood to the 1 mark, and dilute with salt solution of the highest strength. Shake and expel the fluid into a small test-tube. Make similar dilutions with each succeeding strength of salt solution. Place the rack of tubes in the incubator for one hour or in a water-bath at 37° C. for one hour. Note in which tube hemolysis begins and in which tube hemolysis is complete.

diagnosis. We must differentiate the disease from five other conditions especially, *i. e.*, first, from profound secondary anemia of a pernicious type due to carcinoma, ova parasites, infections, nephritis, pregnancy, or toxins. Second, from cardiovascular disease. Third, from gastro-intestinal disturbances. Fourth, from posterior or lateral sclerosis or posterior lateral sclerosis. Fifth, from chronic hemolytic jaundice. The blood-picture is, of course, the most important single point in each case.

The patient suffering from secondary anemia is usually a different looking individual—he has lost more weight, he looks less well nourished, he has a different pallor, and in him we can find some etiologic factor responsible for the disease, and when it is removed the anemia is curable. So long as we can find no etiologic explanation for the condition it is a pernicious anemia. The blood-picture may be that which I have described as characteristic of pernicious anemia or it may be that with which we are all familiar, a striking achromia—*i. e.*, the cells are pale and vary in depth of staining. The cells are quite uniform in size, though they may vary in shape. The reticulated red cells are usually normal in number. The white cells vary according to the cause of the disease, as do the polymorphonuclears. Normoblasts and megaloblasts may both be present, but large oval cells and numerous macrocytes are conspicuously absent. The ordinary laboratory technic for gastric and urine analyses, stool examination, etc., which I have emphasized above and which would be applicable to the study of any possible underlying cause must be employed.

In chronic hemolytic jaundice there is usually a real icterus and an enlarged liver and spleen. The blood-count and smear may be identical with that of pernicious anemia, but reticulated red cells are greatly increased, averaging 15 to 20 per cent. The resistance of the cells to different strengths of salt solution is much decreased, the hemolysis beginning at 0.7 per cent. and complete at 0.46 per cent. In pernicious anemia the figures may be normal or slightly increased or decreased. To make a correct differentiation between these two diseases is very important, as the hemolytic jaundice is curable by splenectomy.

The differential diagnosis in the other diseases is obvious. I mention them only in order that we may not make an error by sheer negligence and carelessness.

The prognosis must be guarded. There may be half a dozen remissions and it is not uncommon for them to cover a period of ten years or even twenty. Osler says that patients usually survive the first two remissions. The average duration of life after diagnosis is made is two and a half years. These remissions come and go in patients that are under treatment and in those who are under no medical care. We have already emphasized the difficulty of correlating any relationship between different forms of treatment and improvements. In the same patient a blood transfusion or arsenic or iron may at one time seem to be useless, again we think they stimulate a remission, and then again, when the patient is discouraged and out from under your care, he suddenly starts to improve and gains faster and more than he has at any time under strenuous treatment.

We have not only to forecast the possible prognosis for life but also the duration of individual symptoms with relation to the blood-picture. You may tell a patient his hemoglobin is 90 per cent., but this is little comfort to him if he has a sore tongue, or numbness and tingling in his feet and hands, or a tabetic gait. When will these disappear? The answer is, You do not know. They may disappear at any time and they may persist into another crisis.

Arsenic, as sodium cacodylate, if given hypodermically in doses of $\frac{1}{2}$ to $\frac{3}{4}$ grain three times a week for two or three weeks, seems at times to stimulate the production of red blood-cells as we pointed out in the case described. Subjectively patients are better when being treated, even though the blood-picture does not alter.

Of just how much value iron is we do not know. It has seemed to us that patients improve as much without it as with it. After all, the need is for more cells rather than more hemoglobin.

Transfusion is the most helpful procedure—it does not cure, but it seems to stimulate the bone to throw out younger cells more rapidly and more surely than any other procedure.

The question of when to transfuse, what volume of blood to give, how often to repeat, what donor to use, must all be decided.

Finally, splenectomy must be considered. Its advocates do not claim that it cures the disease. Minot and Lee state that in those cases with large spleens it does result in the stimulation of the bone-marrow and that 70 per cent. get relief temporarily. When it is recommended the patient should be warned that it is not without a real risk, for a goodly percentage get thromboses of the abdominal or femoral veins which are often fatal.

In those cases with marked nausea and vomiting great benefit and comfort is derived from intravenous injections of 10 per cent. glucose solutions. We give 250 c.c. once a day and thus furnish the patient with 100 calories. In addition, we have found that rectal feeding makes the patients more comfortable and helps tide them over their period of vomiting. These enemas were suggested by Dr. Helen Baldwin at the New York Infirmary for Women and Children. We tried daily small plain enemas followed after the evacuations were completed by a nutrient enema of

Peptonized milk	℥viij—calories, 160
Levulose	℥ij —calories, 240
Liquid peptonoids	℥j

We have several times controlled nausea in this way.

The question of transfusion must include a consideration of the donor first of all. Dr. Lindeman used to say that the ideal donor was a large man of 160 to 170 pounds, not fat, who had large veins, and no nerves, who had no tuberculosis, no history of syphilis, a negative Wassermann.

The first test to be made is a Wassermann on the donor's blood and then a careful test for compatibility. Short cuts to these tests are poor. Dr. Lindeman always emphasized the importance of doing the macroscopic test and reading it not only at the end of two hours' incubation period but also after letting it stand twelve hours in the ice-box. In case the same donor is used for further transfusions never neglect repeating the same tests with equal care. The amount of blood to be used

is always a question. It has seemed to us that small quantities (300 to 500 c.c.) are as effective in pernicious anemias as 1000 to 1500 c.c. What we are after is stimulation of the bone-marrow, and unless the patient is desiccated we believe in the smaller quantities. The method to be used is also a question. Direct transfusion is the method of choice and the ingenious apparatus of Unger makes the technic very simple. The Lindeman method is excellent, but the procedure is more clumsy than that of Unger. The chief objections to either is the expense of the apparatus.

When direct transfusion is not feasible the citrate method is a satisfactory substitute and requires no expensive apparatus. An ordinary infusion or salvarsan set suffices.

What occurs during and after a transfusion? In case all goes well the color of the patient becomes more normal. The green tint is replaced by a decided pink. The pulse is slower, softer, and frequently dicrotic. The patient feels drowsy and often sleeps for several hours and wakes up feeling hungry.

In case of unfavorable reactions the patient gets pale, cyanotic, dyspneic, yawns, and feels chilly. The pulse becomes more rapid and thready and respiration may cease. At the first indication of any of these symptoms the procedure should be interrupted and, if necessary, a hypodermic of 15 minims of adrenalin given and external heat applied.

After the transfusion the temperature, pulse, and respiration should be taken every half-hour. In about 10 per cent. of the cases of direct transfusion and in 35 per cent. of the citrate cases there is a reaction similar to that following an infusion of salt solution or salvarsan, *i. e.*, a chill, a rise of temperature, nausea, vomiting. This is no cause for alarm and will last only twelve to twenty-four hours.

The cause of this is conjectural, but it is believed to be a protein reaction. In 10 per cent. of the cases there is a skin eruption of an urticarial type that is very annoying. It may be alleviated by the application of a 1 per cent. solution of benzyl alcohol.

In cases of incompatibility, where the blood is not tested

or not tested properly, there is either a hemolysis or an agglutination. In some cases which have been most carefully tested similar reactions may occur. Isohemolysis is only 20 to 25 per cent. as frequent as iso-agglutination. With hemolysis there may be restlessness, chills and fever, delirium, convulsions, increased hemoglobinuria or hematuria, hemorrhages from the mucous membranes or into the skin, jaundice. The onset of the reaction may be very sudden and may eventuate in death.

In some cases we get reactions where our tests for hemolysis and agglutination are all right. Hooker suggests that there are causes for disturbances of which we know nothing—disturbances of physiologic balances or toxic biological reactions for which we have no tests. Furthermore, the blood of the donor may undergo incipient coagulation changes due to the physical influence of transference, and though these changes are insufficient to cause coagulation, they may be sufficient to cause a toxic disturbance in the recipient's circulation.

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THE PRINCIPLES UNDERLYING THE TREATMENT OF THE DIARRHEAS

THE therapy of the diarrheas is steadily emerging from a purely empiric to a more scientific basis. The most recent advances in this field include a much more skilful and exact employment of diet than in the past, a more precise utilization of many old and some new drugs, and the introduction of trans-intestinal flushes. In any attempt at presenting this subject so many varieties of the disease must be considered—for the diarrheas are, of course, the result of manifold causes—that it will make for clearness if a reasonably comprehensive scheme of classification be followed. The accompanying chart offers, it is hoped, a rational grouping of the forms of diarrhea most commonly met with.

A CLASSIFICATION OF THE DIARRHEAS

A. Functional:	B. Organic:
I. Simple or environmental.	I. Toxic:
II. Gastrogenous	1. Mercury.
	2. Arsenic, etc.
III. Putrefactive.	II. Infectious:
IV. Fermentative.	1. Specific or primary:
	(*a*) Bacillary:
	Cholera.
V. Endocrine:	Dysentery.
1. Thyroid.	Tuberculosis.
2. Adrenal.	(*b*) Protozoal:
	Amebic.
VI. Pancreatic.	Flagellate.
	2. Non-specific:
VII. Sprue.	(*a*) Secondary to any of the above, whether functional, organic, or due to new growth.
VIII. Nervous.	(*b*) "Ulcerative colitis."

It will be seen from the above chart that all diarrheas may be divided into two great groups—functional and organic. This division, here as elsewhere in gastro-enterology, is of immense clinical importance, inasmuch as the first practical question to decide before treating any case of diarrhea is whether the process is or is not associated with a demonstrable lesion or infection of the intestinal tract.

The differentiation between these two chief divisions is not difficult. If the stools contain blood, pus, and mucus, with or without specific infective organisms, and if endoscopic examination of the lower bowel shows actual inflammatory or ulcerative changes, the diagnosis of organic disease is established. Other confirmatory features of organic diarrheas are: Continuous, as opposed to an intermittent flux (though this is not universal), persistent pain and tenderness along the course of the colon, positive Roentgen findings, and signs of systemic involvement—cachexia, anemia, fever, and severe emaciation.

If, on the other hand, the course of the disease is self-limited, or else intermittent with periods of health between the exacerbations (also not universal), if the stools are persistently free from blood, pus, mucus, and specific organisms, if the endoscopic and Roentgen examinations are negative and the general condition fair or but little affected, the case in question is to be regarded as functional in nature.

GENERAL PRINCIPLES OF TREATMENT

The generally recognized principles governing the treatment of all forms of diarrhea may be summarized under the following heads:

1. General body rest.
2. Diet.
3. Specific measures.
4. Local or topical treatment.
5. Drug treatment.

1. **Rest.**—General bodily rest is practically the first measure to apply in the treatment of any case of diarrhea. This is because rest in bed—which is, of course, the most effective way

of resting—decreases all smooth muscle activity, and specifically, all peristaltic action. It is a common observation that diarrheas are less active at night, and this is not only because food is not ingested, but because of the customary repose during this period. In functional cases particularly there may be no evacuations whatever during the night hours.

Rest in bed for a period of twenty-four to forty-eight hours may be the only treatment necessary for the control of many mild cases of diarrhea. In this connection it may be stated in a general way that if a flux persists despite a period of bed rest plus appropriate dietetic management the case may be regarded as probably organic in nature.

Various physical methods of treatment can be conveniently combined with bed rest. Among these the simplest is the application of heat for the purpose of diminishing peristalsis and controlling colic and abdominal discomfort in general. Wet heat is administered in the form of compresses or poultices. Dry heat may be applied in the form of the hot-water bag or, better still, by means of the electric pad or heater.

Other physical measures of possible usefulness are direct sunlight and the quartz (Alpine sun) lamp. These have been recommended particularly in the severe forms of enteritis, such as that due to tuberculous infection.

2. **Diet.**—It is self-evident that the food should be well subdivided, free from irritants, and readily assimilable. Only the best quality of food-stuffs should be selected and the cooking should be as thorough and skilful as it is possible to make it. Vegetables and cereals should be well mashed, strained, or passed through a purée sieve. All residue-containing foods (fruits, coarse vegetables, etc.) and all irritating and stimulating substances, such as spices, alcohol, etc., should be avoided. Careful and deliberate chewing is of the first importance and the teeth should, of course, receive proper attention.

In most acute diarrheas, and at the beginning of treatment in many of the chronic forms, provided the patient's condition allows it, a starvation period of twenty-four to forty-eight hours may materially aid in hastening recovery. This rest interval

may be preceded by a quickly acting, smooth purge, such as castor oil, in order to insure the elimination of all irritating or fermenting products that may be present in the intestine. During the fast thirst may be allayed by allowing the patient to suck small pieces of ice at frequent intervals, or, in more serious cases, by administering fluids under the skin or into the veins. When the acute symptoms are over, as determined by the diminution or disappearance of colic, peristaltic unrest, and frequent bowel movements, feeding may gradually be resumed according to the plan selected (see following sections).

Of the greatest usefulness in the study of the chronic diarrheas, particularly of the functional variety, is the intestinal test diet introduced by Adolf Schmidt.[1] This diet takes the same place in the investigation of intestinal disorders as does the Ewald meal in testing out the functional capacity of the stomach. The Schmidt diet is so well balanced as regards its composition in the principal basic food-stuffs that the normal intestine digests these substances without the appearance of excessive residues in the feces. On the other hand, should examination of the stools reveal undigested meat, fat, or starches after a three-day Schmidt regimen it is safe to assume that the diarrhea in the case in question is due to an inability to handle the class of food-stuffs that appear unchanged in the excrement.

SCHMIDT INTESTINAL TEST DIET

Breakfast:

One pint of milk, or tea or cocoa, prepared with much milk.
One buttered roll.
One soft egg.

10 A. M.:

One large plate of thick oatmeal soup, strained, cooked with milk and water, and flavored with sugar or salt.

Dinner:

One large plate of thick potato soup.
One-quarter pound chopped or scraped beef, slightly browned in the pan.

4 P. M.:

Same as at breakfast without the egg.

Supper:

Same as at 10 A. M., with one or two buttered rolls, and one or two soft or scrambled eggs.

[1] Schmidt, A., Die Funktionsprüfung des Darmes mittels der Probekost, etc., 2d ed., Wiesbaden, Bergmann, 1908.

Not only is the Schmidt diet of value in diagnosis, but in some of the diarrheas, particularly the fermentative, it has real therapeutic value as well. Ofttimes the diarrhea disappears entirely by the time the test is completed, or the flux is so reduced in degree that but few further changes are required in the feeding program tosecure a completely successful result.

Other special diets of value will be discussed under the particular forms of diarrhea to which they apply.

3. **Specific Measures.**—Where there is lack of some of the digestive secretions a specific replacement or substitution therapy is in order. The use of hydrochloric acid in the diarrhea of achylia gastrica comes under this head. In cases of pancreatic insufficiency the administration of the missing ferments is similarly indicated.

Still another form of specific therapy is that directed against certain of the infective organisms which cause diarrhea. Among these are the dysenteric amebæ, the dysenteric bacilli, and some of the flagellate protozoa. Treatment of parasitic worms, when these cause diarrhea, may also be considered to come under this head.

4. **Local Treatment.**—The object of local intestinal treatment is threefold, viz., to clean out the bowel of irritating or infectious material, to overcome infection through antisepsis, and to soothe or allay intestinal irritability. For gross cleansing purposes the use of a smooth cathartic, such as castor oil, as already mentioned, is of acknowledged value. Recently the use of transintestinal flushes is coming into vogue. By this means the entire intestinal tract is slowly irrigated from above downward with fairly large quantities (1000 c.c.) of hot hypertonic saline solution (0.9 per cent. each of sodium sulfate and sodium chlorid).[1]

Gross[2] was the first in this country to advocate the use of oxygen insufflations through the duodenal tube in cases of fermentative and putrefactive intestinal dyspepsia.

[1] Jutte, M. E., Auto-intoxication and its Treatment by (Trans-)Duodenal Lavage, Amer. Jour. Med. Sci., 153, 732–738, 1917.

[2] Gross, M. H., Disinfection of the Intestines by Insufflation of Oxygen, Medical Rec., 82, 986–990, 1912.

All sorts of cleansing and medicinal irrigations have been recommended for use per rectum. These will be considered in some detail in the section on the Treatment of Infectious Diarrhea.

For soothing purposes starch and oil injections are of real value. When given at the proper temperature they tend to control tenesmus and colic. The administration of non-cathartic oils by mouth, such as olive oil, also tends to help the healing of lesions in the intestine.

5. **Drug Treatment.**—In most cases of diarrhea medication is really a matter of secondary importance. Drugs are indicated either in very acute conditions with much tenesmus, pain, and choleraic manifestations, or else in the chronic forms of diarrhea as aids to other forms of therapeutics. Occasionally, however, drugs may act in a specific manner—*e. g.*, adrenalin(?).

Medicaments used in the treatment of diarrhea may be considered under two great groups—viz., the common antidiarrheics and the astringents. The antidiarrheics act on the nervous system and the neuromuscular control of the intestine. Opium and its alkaloids produce their effects by depressing the reflex irritability of the intestine to stimuli. The usefulness of drugs of this class is limited in practice, owing to their tendency to increase inflammatory processes by producing undue stasis. These substances find their chief indication in acute, choleraic fluxes.

Epinephrin (adrenalin) stimulates the sympathetic system, the latter acting as an inhibitory mechanism for both intestinal motility and secretion. The drug seems to be particularly efficacious when given locally in enema form. Some very clear-cut results have been reported from its use (see Thyroid Diarrheas, below).

Atropin also acts in an inhibitory way on intestinal motility and secretion, but it does this by paralyzing the vagus nerve endings instead of by stimulating the sympathetic as does epinephrin. Atropin action, however, is not always uniform. Indeed, paradoxic results—*e. g.*, increase in peristalsis—may occur, according to some authorities, from small doses. On the

whole, the successful exhibition of atropin demands considerable clinical experience.

The so-called astringents combine various qualities which make them of considerable value in intestinal therapy. By precipitating albuminoids they increase the consistency of the intestinal content. Furthermore, this precipitating action extends to the superficial layers of the intestinal mucosa, and in this way the latter is protected against chemical, bacterial, and mechanical irritants at the same time that secretion and transudation are markedly diminished. By similarly inhibiting the intestinal bacteria and the bacterial toxins the astringents come to exert a specific antiputrefactive and antiseptic action. Finally, by their tendency to cause capillary constriction and to dry the surface of the mucosa the astringents diminish the sensitiveness of the intestine to both direct and reflex stimuli.

Except for its use in the form of tea the classic astringent, tannic acid, has been practically discarded in modern oral therapy. Its place is now taken by the newer preparations, such as tannigen (daily dose 2 to 4 grams) and tannalbin (daily dose 6 to 8 grams), which have the advantage of passing unchanged through the stomach.

Even more useful than the above are the bismuth preparations, since the danger of causing too great a depression of motility (stasis) is less with these than with drugs of the tannic acid class. Bismuth, in addition to its mechanical coating effect has the added virtue of binding H_2S in the intestine and removing this irritant by excreting it in the form of the well-known black crystals of bismuth sulfid. Bismuth subcarbonate is perhaps the best known of the bismuth salts. Bismuth subgallate (dermatol), bismuth tribromphenate (xeroform), and bismuth betanaphthalate (orphol) are some of the more commonly employed newer preparations. The daily dose of each of these is 1 to 3 grams, best given in the morning, fasting, and at bedtime.

The silver astringents, silver nitrate, and the newer protein and colloidal preparations (argyrol, collargol, electrargol, etc.),

are used only for intestinal irrigations. Silver nitrate is employed in strengths of 1 : 5000 to 1 : 3000.

Calcium salts also are astringent and tend to decrease peristalsis. Calcium carbonate (dose 1 gram) is the form most commonly administered by mouth. Where distress is caused by evolution of excessive CO_2 in the stomach the neutral calcium phosphate may be given instead. Greenwald[1] has recently shown that the gastric reaction is much less changed by the latter salt than by the carbonate, inasmuch as the total acidity is little altered (although the free HCl is diminished). The writer's experience with this drug in diarrheas associated with gastric hyperacidity has been encouraging. The dose is 1 to 3 grams three or four times daily.

Calcium chlorid, which is soluble, has been used both for intestinal irrigation in 1 to 2 per cent. solution, and intravenously in 5 per cent. solution (dose 5 c.c.).

In addition to the antidiarrheics and astringents the general sedatives (bromids, chloral, etc.) are deserving of mention. These dependable drugs are of recognized value not only in the nervous diarrheas as such (see below), but in all diarrheas that are associated with a manifest neurotic element.

TREATMENT OF INDIVIDUAL FORMS OF DIARRHEA

A. The Functional Diarrheas

I. Simple or Environmental Diarrhea.—As the name indicates, this form of diarrhea may occur in persons with perfectly normal intestinal tracts. The disorder is brought on by some entirely extraneous factor, such as ingestion of spoiled or unripe foods, heat-stroke, preventive inoculation, etc. The ordinary summer diarrhea and "acute gastro-enteritis" is generally of this character. The treatment is very simple indeed. Bed rest, abstinence from food, in some cases a rapid purge or enema, is all that is needed. Medication with bismuth or chalk mixture is unnecessary, as recovery is just as rapid without drugs. Feeding may be recommenced with tea or milk. Many patients

[1] Greenwald, I., Personal communication.

will be found to prefer orange juice or other fresh fruit juices, as they are refreshing and generally well-borne and tend to prevent acidosis. After a day or two gruels, cereals, toast, and then various soft vegetables, fish, and chicken may be given.

II. **Gastrogenous Diarrheas.**—Three varieties of gastrogenous diarrheas may be distinguished.

1. *Diarrhea With Achylia Gastrica.*—This form is treated by appropriate (bland) diet, by the administration of hydrochloric acid, and by the control of intestinal dyspepsia. For details of these procedures reference should be had to appropriate works on the subject.

2. *Diarrhea With Gastric Retention (Delayed Gastric Emptying).*—It is an old clinical observation that when food stays too long in the stomach from any cause it is likely to stagnate or ferment, with the result that whatever chyme goes through the pylorus tends to set up an irritation of the intestines that may result in diarrhea. The principles of treatment are those applicable in general to the condition of delayed gastric emptying, viz., feeding in proportion to the ability of the stomach to empty itself, frequent aspirations of old gastric residues followed by lavage, administration of antispasmodics and of alkalies to reduce hyperchlorhydria, where this is the cause of pylorospasm, gastro-enterostomy in advanced cases, etc.

3. *Diarrhea from Malfunction of Gastro-enterostomy.*—The most common condition under which diarrhea occurs following gastro-enterostomy is where the stoma is so large that the stomach empties with unusual rapidity into the intestine. The irritation thus produced causes increased peristalsis throughout the remainder of the intestinal tract. The cure for this condition is very careful feeding of small amounts of food, followed by rest in the reclining position after each meal. Preceding the feeding small doses of bromid may be helpful.

In cases where the stoma is so large or so placed that complete neutralization or even alkalinization(?) of the gastric contents occurs a condition is produced closely akin to achylia gastrica. In this contingency the administration of hydrochloric acid is indicated in much the same manner as for a true achylia.

III. **Putrefactive Diarrhea.**—This form of diarrhea is commonly intermittent in occurrence. It is associated with an inability on the part of the intestine to digest protein food-stuffs. The stools are fluid, foul, alkaline in reaction, and contain undigested food particles, particularly raw connective tissue after a Schmidt diet. Often there is a high indicanuria. The fermentation test is negative—*i. e.*, large quantities of gas are not produced and an acid reaction is not obtained after the incubation of a stool (following the test diet) in a Schmidt fermentation apparatus for twenty-four hours. Putrefactive diarrhea is often associated with achylia gastrica.

The treatment of this condition is based on the exclusion from the diet of food-stuffs which (1) introduce putrefactive or putrescible material into the intestines; (2) sharply stimulate intestinal secretion; or (3) increase the peristalsis of the small intestine. With these principles as a basis Schmidt and von Noorden[1] recommend the following plan of feeding:

Diet in Putrefactive Diarrhea.—First Stage.—Starvation for one to three days. In mild cases 5 ounces of weak tea may be given every two to three hours. In severe cases nothing by mouth. The fluid requirements of the body should be supplied by the subcutaneous or intravenous injection of 5 per cent. glucose solution.

Second Stage.—Three to four days of sugar-water. This is given as a 10 per cent. solution of sucrose in boiled water or weak tea; 5 to 10 ounces are administered five to seven times daily.

Third Stage.—This consists in the gradual replacement of the sugar-water with boiled milk or fermented milk products, such as fermillac, zoölak, etc. By the second week the patient should be getting from 1½ to 2 liters of milk food daily and the sugar-water may be omitted. During this period cream may be added carefully (up to 8 or 10 ounces daily) in order to increase the caloric value of the diet.

During the second week small amounts of pot cheese may be added, since it has been shown that the lactic acid bacteria already introduced with the milk are sufficient to prevent putrefaction of this particular type of protein. Some of the milk may now be replaced by Nestle's food or malted milk, by barley or oatmeal gruel, and by gruels made of the finer starches, such as arrowroot or cornstarch. Feeding is to be carried out every two hours.

As an alternative to the milk diet outlined above one may proceed with toasted bread made of the finest wheat flour, allowing 2 to 3 ounces six to seven times daily, and only so much tea as will satisfy thirst. Or else 2 ounces of

[1] Schmidt, A., and Von Noorden, C., Klinik der Darmkrankheiten, 2d ed., Munich, Bergmann, 1921, p. 299 ff.

the best quality of cooked rice may be given at each feeding, prepared with a minimum amount of water.

Fourth Stage.—All of the above items may now be given in combination, viz., milk and milk preparations, cream, pot cheese, gruels, rice, and toasted white bread. The vegetable proteins (legumes, such as peas) are next to be added, then eggs, and finally chicken, fish, and meat.

Alcoholic drinks, such as red wines and spirits are allowed, where necessary, in all stages. In the mild cases normal diet may be resumed in two to three weeks; in the severe cases, in four to five weeks.

IV. **Fermentative Diarrhea.**—In this form of diarrhea the intestine is unable to digest starches, particularly when the starch cells are enclosed in vegetable cell membranes or envelopes. The stools are large, pultaceous, light colored, frothy, sour smelling, and acid in reaction. Stool examination after the Schmidt test diet shows numerous starch cells and the presence of characteristic granular spore-bearing bacilli. The fermentation test shows the production of large quantities of gas.

The object of therapy is to free the intestine as much as possible of all acid- and fermentation-producing bacteria. To this end all carbohydrates are excluded from the diet. The regimen prescribed is very similar to that used in diabetes, with the additional restriction that here even the carbohydrate-poor vegetables, such as the greens, are also eliminated. The details of feeding are as follows (modified from Schmidt-von Noorden):

Diet in Fermentative Diarrhea.—First Stage.—This stage lasts from six to ten days. A preliminary fast period of one to two days is always desirable.

Breakfast: Eight to 10 ounces of protein milk.[1] Two soft boiled eggs.

10 A. M.: Five to 6 ounces of fresh pot cheese, to which may be added after a few days an ounce of fresh butter. One cup of beef-tea.

Dinner: Beef-tea or beef-tea jelly. Fine well boiled, roasted, or pot roasted meat, or boiled or broiled fish with drawn butter. Red wine. Jell-O (wine or lemon flavor, sweetened with saccharin).

4 P. M.: Ten ounces of protein milk. One soft egg.

[1] Protein milk is prepared as follows: To 1 quart of milk add 1 teaspoonful of Simon's essence of rennet (or a similar amount of any other standard ferment). Place in water-bath at 42° C. for a half hour. After the coagulum of milk is formed put it in cheese-cloth and let it strain slowly by gravity for an hour. Then remove coagulum and place it in a very fine sieve, and while washing with 1 pint of water force coagulum slowly through the sieve by means of a wooden spoon. This procedure is repeated several times. To the finely divided coagulum now add 1 pint of buttermilk. The whole may be sterilized by boiling.

Supper: Two eggs scrambled in butter. Fine chopped chicken. One ounce of cheese, or Jell-O as at noon.

Note: Acetonuria may appear during this stage, but according to von Noorden it is harmless and ceases after two to three days.

Second Stage.—Gradual addition to the above, in small quantities, of corn and arrowroot "blanc manges," strained oatmeal and barley gruels, or, if these are unavailable, infant foods, such as Nestle's. Small amounts of sugar may be added as desired.

Third Stage.—Replacement of the protein milk with increasing amounts of fermented (*i. e.*, lactose-poor) milk such as kefir or zoölak or fermillac, and later with whole milk. Gradual addition of fine wheat products, such as zwieback, toasted white wheat bread, and sponge cake made of wheat flour, butter, sugar, and eggs. Next are added fine puréed (strained) vegetables, such as spinach, young carrots, young kohl-rabi, etc. Following this mashed potato and apple sauce may be given. Butter may now be taken freely. All the above vegetables contain at most small quantities of cellulose. The following menu may now be ordered:

Breakfast: Tea with milk and sugar, or cocoa with milk. Toasted white bread with butter. Two soft or scrambled eggs.

10 A. M.: 10 ounces fermented milk or whole milk. Toast or bread with butter.

Dinner: Beef-tea with or without fine cereal flour (rice flour, farina, cream of wheat). Finely chopped meat or fish, later with mashed potato. Puréed vegetables. Toast with cheese and butter. Dessert of Jell-O; later apple sauce.

4 P. M.: Milk or milk modification. Toast with butter.

Supper: Scrambled eggs. Toast with butter and pot cheese. Warm or cold meat or fish.

10 P. M.: Milk or milk modification.

Fourth Stage.—During this period the bowel is trained, under the most careful supervision, to handle material containing crude fiber (vegetable cell wall membranes). It is best to begin with wheat bread and well-cooked porridges made of such cereals as oatmeal, barley, rice, wheatena, cornmeal, etc. Later boiled or baked potatoes may be given. Other stewed or canned fruit may now be added in addition to apple sauce. Finally, coarser breads, such as graham, or whole wheat, and raw fruit may be tried if the patient so desires.

Mixed Forms (*Putrefactive and Fermentative*).—Here a preliminary starvation period of two to three days serves to control both the putrefactive and the fermentative dyspepsia. This should be followed by a two- or three-day period of sugar-water feeding as in the second stage of putrefactive dyspepsia. After this an abrupt change should be made to the first stage of the fermentative diarrhea regimen (protein milk, eggs, cheese, butter, beef-tea). From this point on no further rules can be laid

down, as the treatment must be empiric. Most of the cases are not simple dyspepsias (functional), but are really instances of enterocolitis (organic).

V. **Endocrine Diarrheas.**—The diarrheas of both Addison's disease (adrenal insufficiency) and Basedow's disease (hyperthyroidism, thyreotoxicosis) resemble each other clinically. The onset is sudden, the stools are watery and contain mucus and bilirubin (an indication of insufficient reduction of bile-pigments to the normal state of hydrobilirubin), and the attacks often end as abruptly as they commence. In both these types of diarrhea very satisfactory results are reported from the use of suprarenal substance by rectal injection[1]; 25 to 30 drops of the 1:1000 solution of adrenalin chlorid are given in 200 to 300 c.c. of water. It is safe to repeat such an enema several times daily, as it has been shown that adrenalin, when applied intra-intestinally, has no systemic action whatever. As a matter of fact, however, a second injection in the twenty-four hours is seldom necessary, inasmuch as ordinarily no stools are passed from fifteen to twenty-four hours following the treatment. The author's personal experience with this method, though limited to date, has been very satisfactory.

Lately Shapiro and Marine[2] have obtained relief of diarrhea in Basedow's disease from the use by mouth of a glycerin extract of suprarenal cortex. This preparation has the added advantage of exerting a markedly beneficial effect on many of the other symptoms of the disease.

VI. **Pancreatic Diarrhea.**—In deficient external secretion of the pancreas (obstruction to the duct of Wirsung) the stools are characteristically bulky and foul and contain large amounts of unchanged (neutral) fat and meat fibers (steatorrhea and creatorrhea, respectively). The only treatment for this condition is the administration of pancreas "extract." Sometimes the commercial preparations—*e. g.*, pancreatin—prove effective, but when these fail an attempt should be made to secure fresh

[1] Eppinger, H., and von Noorden, K. H.,.Zur Therapie der Basedowschen Diarrhöen, Internat. Beitr. z. Path. u. Ther. d. Ernährungsstör., 2, 1–6, 1911.

[2] Shapiro, S., and Marine, D., Personal communication.

pancreas tissue from the abattoir. This may be administered either raw in chopped (sandwich) form, or as a glycerin extract of the whole gland.

VII. **Sprue.**—So long as the exact etiology of this disease is still not definitely agreed upon, it seems best to include the condition among the functional diarrheas. The stools in sprue are very distinctive. They are passed most often in the morning, are not usually accompanied by pain or tenesmus, and seldom exceed two or three in number in the twenty-four hours. The movements are very copious, foamy, and vary from pultaceous to fluid in consistency. The smell is penetrating and the reaction always sour. Their color is characteristic, namely, a light yellow or brown, due to their large fat content and to the presence of leukobilirubin, a reduction product of hydrobilirubin. The excess of fat is due to fatty acids and soaps; the neutral fat output is not increased.

For the treatment of sprue three different plans of feeding are in vogue, namely, the "strawberry" diet, the "milk" diet, and the "meat" diet. The effect of strawberries is said to be almost specific, and improvement is so striking that these berries may be used as a therapeutic test. When used to effect a cure the berries may be given in gradually increasing amounts daily. Milk may readily be combined with the strawberry diet. Bananas and other fruit are also commonly added.

The milk diet as practised by Ashford[1] consists of 8 ounces of milk every two hours, nine feedings in twenty-four hours, increasing the feeding by 1 ounce every four days until 13 ounces are taken every two hours for one week. The milk should be taken cold through a straw. To the milk is added one-half a culture tube of Bacillus bulgaricus to each feeding. When 13 ounces are reached, one banana is added to the day's feed, and every fourth day one more is added for every ounce of milk to be subtracted per feeding. When 10 ounces of milk every two

[1] Ashford, B. K., Relation of the Genus "Monilia" to Certain Fermentative Conditions of the Intestinal Tract in Porto Rico, Jour. Amer. Med. Assoc., 64, 1893–96, 1915. The Dietetic Treatment of Sprue, Amer. Jour. Trop. Dis. and Prev. Med., 3, 377–389, 1915–16.

hours and 3 bananas a day are reached, the diet is usually modified to include eggs, fruit, and vegetables with a low carbohydrate content.

The meat diet is preferred by some and is certainly to be employed whenever milk is unavailable or is objected to. E. J. Wood[1] employs a "strict beef diet to which are added copious drafts of hot water. The beef is deprived of fat and fiber and is then carefully chopped, but never ground. It is made into balls which are very lightly cooked on a hot iron. From 8 ounces to 2 pounds divided into four portions are given in twenty-four hours." The effect on the anemia as well as on the diarrhea is said to be striking. Small portions of toasted bread crumbs are added to the beef diet. After a while fruit and vegetables are introduced and the beef may be gradually withdrawn.

VIII. **Nervous Diarrhea.**—It is important not to classify as purely nervous those diarrheas which may occur in neurotic individuals, but which are really due to some form of intestinal dyspepsia. For true nervous diarrheas, such, for example, as the fear or anxiety types occurring during periods of great emotional upset, there is no specific treatment. Only a general plan of management such as that applicable to all neuroses can be instituted in these subjects with the hope of building up the general neuromuscular control and diminishing undue irritability. Mild attacks may be warded off or cut short under favorable conditions by the exhibition of sedatives, such as bromids, chloral, or codein.

B. The Organic Diarrheas

I. **Toxic Diarrheas.**—The toxic diarrheas originate from the excretion into the intestine of various drugs when given in poisonous doses. These drugs may be administered by skin (inunction, hypodermic injection) or into the blood-stream (intravenous injection) as well as by mouth. The drugs most commonly responsible for the production of an enteritis of this type

[1] Wood, E. J., Article "Sprue," Nelson Loose Leaf Medicine, New York, 1920, vol. 5, p. 468.

are those used in the treatment of syphilis, namely, mercury and arsenic (arsphenamin). The former drug is not infrequently used for suicidal purposes.

In regard to treatment it is important to recognize the fact that the diarrhea is protective in nature in such cases, inasmuch as the bowel furnishes the chief if not the only effective means of eliminating the poison. Not only, therefore, should such diarrheas not be checked, but further intestinal elimination should be stimulated by catharsis and colonic irrigations until it is certain that the noxious factors have been removed. After this has been accomplished the remaining enteritis should be treated as any non-specific infection (see below).

II. **Infectious Diarrheas.**—The *diarrheas of cholera and bacillary dysentery* are treated by: (1) rest in bed; (2) emptying the digestive tract by rapid purges; (3) bland diet; (4) intravenous or subcutaneous introduction of saline solution to overcome the tremendous concentration of the blood due to loss of tissue fluids, and (5) specific serum therapy where this is available. For further details of treatment reference should be had to special monographs or to works on general medicine.

In regard to the treatment of *diarrhea due to tuberculous enterocolitis* it is the writer's opinion that much could be done to prevent or mitigate this evil if proper attention were regularly given to the diet, particularly in the early stages of the disease. There is every reason to believe that a serious study of each case of diarrhea in a tuberculous subject made from the standpoint of establishing the exact form of intestinal dyspepsia—whether putrefactive or fermentative—would yield valuable indications for proper dietetic management.

Otherwise the treatment of this form of diarrhea is purely symptomatic. Hot compresses to the abdomen help to promote comfort. Good results have been obtained (Spivak) from the use of direct sunlight (heliotherapy) on the abdomen. The use of the quartz (Alpine sun) lamp is also said to be of palliative value. Relief of the diarrhea has been obtained from the intravenous injection of 5 c.c. doses of a 5 per cent. calcium chlorid

solution. Fishberg,[1] who has recently tried out this method, finds it effective only in cases of early tuberculosis.

The **protozoal diarrheas** are characterized by their tendency to recrudescence after long intervals, sometimes years in duration. This is particularly true if insufficient treatment is given in the early stages of the infection. Before attempting specific therapy in these cases the bowel should be well emptied. Smithies[2] puts the patient on liquid diet for two days before beginning active treatment and orders a glass of citrate of magnesia each morning. In the entameba cases he puts the patient to bed, continues the liquid diet, and applies hot pads moistened in boric alcohol mixture over the abdomen. A 10-grain "alcresta" (albuminum salicylate of ipecac) tablet is given every hour by mouth and $\frac{1}{8}$ grain of emetin hydrochlorid is administered hypodermically every four hours for two days. If the stools show diminution of the parasites the dose of ipecac and of emetin is then reduced by one-third, and this is continued for another two-day period. Usually by the end of the first week the patient is taking 1 to 2 grains of emetin hypodermically daily, as well as 10 grains of "alcresta" ipecac four times daily. The colon is lavaged night and morning with 4 quarts of hot normal saline, or with a solution of quinin (1:3000) and thymol (1:5000) in normal saline.

On the sixth day the patient is put on a fat-free diet for twenty-four hours in order to render the administration of thymol safe. On the seventh day thymol is given in the evening, followed the next morning by Epsom salts. The same combination is repeated, starting on the evening of the tenth day. If parasites are still present after two weeks, Smithies orders a colonic lavage with saline, followed by $\frac{1}{2}$ to 1 liter of commercial kerosene given slowly per rectum and retained for one hour if possible.

The diarrheas caused by the flagellate protozoa, particularly

[1] Fishberg, M., Calcium Chlorid as a Palliative Agent in the Treatment of Intestinal Tuberculosis, Jour. Amer. Med. Assoc., 72, 1882–84, 1919.

[2] Smithies, F., The Frequency of Protozoic Enterocolitis in the Middle West: Clinical Manifestations, Diagnosis, and Treatment, Amer. Jour. Med. Sci., 156, 173–184, 1918.

by Lamblia (also called Giardia), may prove extremely difficult to cure, as these parasites have been shown to lurk for years in the gall-bladder or appendix. Smithies recommends the same general plan of treatment as for amebiasis, but instead of emetin and ipecac he orders evening doses of 5 to 15 grains of calomel, followed by 2 ounces of Epsom salts the next day. The calomel medication is repeated every five days until the stools are negative.

The use of neo-arsphenamin in large doses has recently been urged for the treatment of protozoal infections (Carr and Chandler[1]). Chandler[2] claims that "the successful employment of neo-arsphenamin in the treatment of intestinal protozoal diseases depends entirely upon getting enough of this product, or whatever modification of it reaches the intestine, into that organ at one time to kill whatever organisms may be present. The ability to do this depends on the following factors: the size of the dose administered; the ability of the intestinal wall to secrete the product, and the particular species of organism present. For Giardia, for instance, we have found that in patients twenty-five to thirty years of age, who do not have an intensive intestinal ulceration, three injections of 0.6 gram at five-day intervals is sufficient to take care of the infection. If the secretory function of the intestine is impaired through age or extensive ulceration, a larger dose, at least a larger initial dose (usually 0.9 gram), is required to accomplish the desired result. This system of dosage applies as well to the amebas and to Chilomastix. However, Trichomonas and intestinal spirochetes in every case require maximum dosages, at least for the first injection."

The treatment of **non-specific infectious (including ulcerative) diarrheas** may be considered under the following heads:

1. Diet.
2. Local treatment.
3. Surgical treatment.

[1] Carr, E. I., and Chandler, W. L., The Successful Treatment of Giardiasis in Man with Neo-arsphenamin, Jour. Amer. Med. Assoc., 74, 1444, 1445, 1920.

[2] Chandler, W. L., Personal communication.

1. *Diet.*—The food should be free from coarse particles and irritating factors (spices, acid, etc.) in order to spare the diseased bowel as much injury as possible. Fluids by mouth should be restricted inasmuch as the water-resorptive function of the colon is impaired in these cases. Where insufficient fluids for body needs would result from this deprivation the administration of water parenterically is indicated (saline by hypodermoclysis or intravenously). An associated functional dyspepsia should be sought out by a Schmidt test diet and the feeding modified according to the forms already suggested for the treatment of intestinal fermentation or putrefaction. Olive oil is of real value in these cases, not only because it soothes intestinal lesions, but because, when it is well borne, it aids materially in improving the state of nutrition.

2. *Local Treatment.*—As previously stated, the object of local treatment is to promote intestinal cleanliness by the removal or sterilization of infectious products, and to soothe the areas of ulceration. For cleansing purposes intestinal irrigations are commonly employed. In general, all irrigations are to be given with a double flow tube, and as much fluid is to be used as the patient can stand or until the return is clear and free from traces of feces, blood, pus, and mucus. Plain tap-water may be used or normal saline, or various drugs in solution, such as calcium chlorid, sodium bicarbonate, tannic acid, thymol, silver nitrate, argyrol, potassium permanganate, hydrogen peroxid, etc. Irrigations of ordinary hot water (120° F. as it enters the rectum) are recommended by Logan[1] as being curative in cases of ulcerative colitis when the process is limited to the lower bowel. The irrigations are given twice daily for twenty to thirty minutes. Lime-water is very useful for the disintegration and removal of mucus accumulations.

As a soothing measure retention enemas of starch paste or olive oil are of value. Logan recommends 3 ounces of olive oil and 60 grains of bismuth (subcarbonate) to be given nightly in the knee-chest position and to be retained as long as possible. He also prescribes the same combination by mouth.

[1] Logan, A. H., Chronic Ulcerative Colitis, Northwest Med., 18, 1–9, 1919.

Where the ulcerative process is limited to the rectum, rectosigmoid, or lowermost pelvic colon there is danger that the ordinary colon irrigations may make matters worse by carrying infection from below upward into healthy segments of the large intestine. In such cases one of the following methods of administering local treatment is applicable:

Transintestinal flushes by means of the duodenal or intestinal tube are now being used with some success in cases of intestinal ulceration (Einhorn[1]). This method would seem to be particularly appropriate to those patients who are "tube-broken," *i. e.*, those who can swallow and pass the tube readily beyond the pylorus. By this means flushes can be given in the physiologic direction from above downward. A quart of hot (110° F.) hypertonic saline (Jutte's solution) may be administered slowly over a period of twenty to thirty minutes. If desired, various medicaments—including the new antiseptic dyes, such as methylene-blue or gentian violet—may be added to the flush solution. The treatment is usually followed within an hour by several watery evacuations. The tube may be retained for days without trouble, or it may be reintroduced at intervals. Flushes may be given daily or two or three times a week as occasion warrants.

In cases of infection and ulceration limited to the lowermost bowel insufflations of calomel powder may be made once or twice a day. Soper[2] has pointed out the antiseptic and healing value of this method. A short proctoscopic tube is introduced, and as it is withdrawn a mixture of equal parts of calomel and bismuth subcarbonate is blown in through a de Vilbiss insufflator. The bismuth is added to the calomel to prevent corrosion of the proctoscopic tube. As the insufflation is made the open end of the tube should be kept covered with a pledget of cotton.

Topical applications are, as a rule, unnecessary when insuf-

[1] Einhorn, M., A New Intestinal Tube with Remarks on its Use in a Case of Ulcerative Colitis, Amer. Jour. Med. Sci., 161, 546–550, 1921.

[2] Soper, H. W., Article, "Inflammatory Processes, etc., of the Rectum and Sigmoid," Nelson Loose Leaf Medicine, New York, 1920, p. 415.

flation treatment is given. However, simple chronic ulcers yield to direct cauterization with carbolic acid (Soper).

3. *Surgical Treatment.*—Where the above measures fail to control colon infection and ulceration the advisability of surgical treatment should be considered. Conservative procedures should, of course, be employed first. These are all directed toward securing better cleansing of the large intestine. Both appendicostomy and cecostomy allow of the introduction of a tube for the permanent flushing of the colon (Gant[1]). Lynch[2] prefers an ileostomy for the same purpose. In extensive ulcerative colitis, where practically the entire large intestine has degenerated into a necrotic pus tube, partial or complete colectomy may be attempted (Yeomans[3]). Needless to say such procedures are attended by a high rate of mortality. Yet in extreme cases there may be no alternative.

For the progressive anemia associated with the continuous loss of blood repeated blood transfusions are indicated, and this procedure has been reported as curative in some cases.

[1] Gant, S. G., Surgical Treatment of Chronic Enterocolonic Diarrhea, Jour. Amer. Med. Assoc., 69, 1603–1606, 1917.

[2] Lynch, J. M., McFarland, W. L., and Draper, J. W., Colonic Infections, Jour. Amer. Med. Assoc., 67, 943–948, 1916.

[3] Yeomans, F. C., Chronic Ulcerative Colitis, Jour. Amer. Med. Assoc., 77, 2043–2047, 1921.

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ATROPIN IN THE TREATMENT OF CONGENITAL PYLORIC STENOSIS

THE object of this report is to record several cases of congenital pyloric stenosis treated medically by means of large doses of atropin. This method was first advocated by Dr. Sidney Haas, of New York City, in 1918. Previous to that time atropin or belladonna had been used in cases of stenosis or pylorospasm, but never in the dosage recommended by Haas. It is to his credit to have shown that doses of atropin, previously considered toxic, can with impunity be given even to newborn infants. At the time of his report his successful treatment was questioned by many, some physicians reporting failure to corroborate his results. It has appeared to me that the failures to obtain proper results with this method of treatment were due to a lack of attention to details in carrying it out, and I purposely am inserting complete records of several cases in order that they may act as a guide to others in the treatment of this disease.

The most important factor in obtaining proper results with the atropin method of treatment is the correct understanding of the dosage of atropin. One should convince oneself of the potency of the drug by using only a freshly prepared solution of atropin obtained from a reliable chemist. Since the commonest symptom of pyloric stenosis is the rapid loss of weight, and since the nutrition of the very young infant becomes so rapidly damaged, it is of the utmost importance that the atropin be allowed to become effective as rapidly as possible. This means that once having decided to apply this form of treatment, the minimum effective dose must be rapidly reached. It is a distinct error to prescribe a small dosage of atropin and to leave

the child on this amount of drug for a day or two to await results. Instead of this, the effect of the drug on each feeding rather than on each day should be taken into account. In other words, it is advisable to begin with 1 drop of a 1 : 1000 solution of atropin sulphate in water given with each feeding. If the vomiting is not controlled, an additional drop should be given at the following feeding. In this way, during the course of the first two or three days of treatment, a large dose of atropin may be arrived at. I have prescribed as high as 72 drops of this solution in twenty-four hours; that is, 1/13 grain of atropin.

In the severer types of the disease I have found it much more advantageous to give the atropin by hypodermic injection. The disadvantages of frequent punctures of the skin are outweighed by two advantages: first, we know exactly how much atropin the child is retaining, and, second we are sure that the entire dosage offered is available for the child. If the child is in the hands of a competent nurse there need be no fear of local infections. I have had no case of infection from a hypodermic injection.

It will be found that very different amounts of atropin are necessary in different cases. The first case reported above was relieved by 7 drops of the atropin solution by hypodermic injection before each of the seven feedings—a total of about 1/20 grain of atropin a day. It was necessary to continue this for five days only, when rapid decrease of the dosage was possible. On the other hand, in Case III it was necessary to increase the dosage to 65 drops of atropin, and the drug treatment of this case lasted over a period of fifty days.

As far as the question of the tolerance of the drug is concerned, I have been guided chiefly by the flushing of the skin. When this becomes very marked soon after a hypodermic injection of the drug the dosage should be considered sufficient or slightly excessive. That the atropin acts in an absolutely definite manner in these cases is very beautifully illustrated by Case II. With this child, who presented an absolutely typical clinical picture of stenosis, including a definite palpable tumor, the atropin was withdrawn several times during the course of

the treatment purely for experimental reasons. Curiously enough, the first symptom which the withdrawal of the atropin elicited was extraordinary restlessness and continuous crying. During these periods of restlessness the vomiting increased considerably and the constipation returned. The child would scream as if in pain and keep jerking its arms and legs about as in an attack of severe colic. During these exacerbations sleep was practically impossible for the baby. It was interesting to note that with a single dose of atropin these symptoms would at once subside, the vomiting would stop, the restlessness disappear, and the baby would drop off into a quiet sleep. This result was so striking that it was demonstrated three or four times in order to make sure that we were not dealing with a coincidence. There is no question that in this case atropin must have relieved pain, for in no other way can its sudden sedative action be explained.

It will be noted that in cases that are recovering the atropin is gradually diminished rather than suddenly stopped. In some cases we were able to have the child discontinue the drug within ten days from the time it was taking the maximum dosage. In other cases a considerable time elapsed before the child stopped taking the drug altogether.

It is a mistake to believe that one can cure pyloric stenosis with atropin alone. This is no more possible than curing it by operation alone. In other words, the atropin is merely useful in removing the spasm which prevents the food from passing out of the stomach, and it is necessary to summon to our aid every other possible factor which can help in maintaining the nutrition of the baby. The very best type of trained nurse is necessary. When we have had occasion to treat these cases in a hospital ward we have asked the hospital to supply a special nurse to look after the wants of this baby only. The questions of amount of feeding, frequency of feeding, and character of the food offered must be carefully considered. Some of the cases treated were breast fed; others were fed upon evaporated milk solutions, and still others upon the thick cereal feedings. It is not my purpose to go into the question here of the proper food

for these infants. This must be left to the discretion of the physician treating each case. Nor have I found that cases improve more rapidly with atropin when on any particular kind of diet. It may be found advisable in some cases to make use of gastric lavage before each feeding. In other cases where the child was very weak gavage was found helpful. Above all, it is necessary to supply sufficient fluid. This may be done in three ways: first, by administering water by mouth; second, by subcutaneous injection of normal saline solution; third, by rectal administration by means of the Murphy drip. In very debilitated infants transfusion of blood may be advisable.

From the above it will be evident that atropin must be considered the most important part of the medical treatment of pyloric stenosis, but by no means the only treatment, and that the many details concerning warmth and feeding and hygiene must be looked after with the utmost care.

What is the value of the atropin treatment as compared with other methods? As far as other medical methods of treatment are concerned, as was pointed out above, atropin must be looked upon as an adjuvant rather than as a substitute. For example, it may be combined with the thick cereal method as advocated by Sauer, of Chicago. The real value of the method seems evident when one considers that by its use surgical operation may be avoided. Some may question the advisability of dispensing with surgical aid when the recent results of surgical treatment of this disease have been so brilliant. However, one must realize that successful surgical treatment of pyloric stenosis is possible only in the hands of a very few of the most skilful surgeons. Moreover, there is always the gravest risk connected with any surgical procedure; especially is this the case in these greatly emaciated, debilitated infants.

The contention has been raised that the atropin treatment would be successful in only moderately severe cases, and that the very seriously sick ones would finally come to operation in any event. However, a case such as that reported by Haas (Jour. Amer. Med. Assoc., October 14, 1922) refutes this statement. This baby was treated at Mount Sinai Hospital on the

pediatric service of Dr. Henry Heiman. It was four weeks old and weighed but 4 pounds and 9 ounces. It was in such a terrible condition that we were afraid to advise surgical intervention. Not only did this child have a distinct stenosis, as was evidenced by a bismuth radiograph, which showed absolutely no food leaving the stomach even four hours after feeding, but it also showed physical signs of a bronchial pneumonia. After atropin had been used for a few days the condition of the child improved slightly and the surgeons were willing to accept the case for operation. However, medical treatment was persisted in and the child recovered completely. This baby was recently seen, and at the age of one year was in perfect health and good condition.

The question as to whether we are dealing with cases of stenosis or spasm is one about which there already has been too much controversy. Advocates of the surgical treatment of this disease have claimed that atropin could only possibly benefit cases of pyloric spasm, but could not possibly be of advantage where true stenosis existed. How we are to differentiate between true stenosis and severe spasm is impossible to decide. Of the 4 cases here reported, 2 had distinctly palpable tumors. The presence of the tumor in Case III was confirmed by Dr. L. E. Holt. This child was particularly interesting because it was the second of 2 children of perfectly healthy parents, the older child having shown the same symptoms soon after birth, and having been subjected to successful operation for pyloric stenosis. The tumor in Case II was exceedingly easily felt. The case cited above, in which the radiogram was made, although no tumor could be felt, revealed complete closure of the pylorus four hours after the administration of food.

Contrasted with the advantages of medical treatment, what are its disadvantages? The most important, I should say, is the length of time that may be required before the case is permanently cured. There is, of course, something quite dramatic in the successful surgical treatment of stenosis. The baby which has been vomiting all food offered, that has had no stools for days, may within a day or two begin to eat and retain food. Oc-

casionally one is fortunate enough to obtain a similar result with medical treatment. However, it has been my experience that the complete cure of the illness takes a longer time when thus treated. Another objection that may be raised to this method is that it necessitates such large doses of a powerful drug to be administered to a very young infant. I myself have not seen any harm as the result of the drug. I know of one case which on arriving at the hospital was put upon this treatment, and apparently did well for several days, when it suddenly began to vomit, ran a temperature, and then went into collapse, and died. There is, of course, the possibility that such a death might be attributable to atropin; however, this child showed no symptoms of atropin poisoning. Moreover, a careful perusal of the child's history showed that its food was strengthened very rapidly, and it is much more likely that the death was due to intoxication brought on by a too sudden increase in diet.

This brings up the important point that the tolerance for food in these infants, who have been starved by the stenotic lesion, has been markedly reduced. One must, therefore, be particularly careful in increasing the diet so as not to overstep the limit of the infant's tolerance. This is just as applicable in cases that have been treated surgically as well as in those that have been subjected only to the medical treatment. Sudden death is not at all uncommon as a postoperative accident in these cases.

In conclusion I would say that judging from my own experience every case of congenital pyloric stenosis should be given the benefit of a thorough course of treatment with atropin as detailed above. It is possible that certain cases will fail to yield to this treatment and that surgical intervention may be required. However, such cases, if there be any, must be very few, and I feel certain that in the vast majority atropin treatment, if conscientiously carried out, will yield brilliant therapeutic results.

CASE I

Stanley B. First seen June 24, 1922, aged five weeks.
Family history negative.

Present Illness.—Six days ago began to vomit after nursing. Vomiting was projectile in character and occurred immediately after nursing. One day ago was seen by a pediatrist, who prescribed thick cereal feedings. Today child appeared very sick and had temperature of 102° F.

Physical: Fairly well-developed male infant showing considerable loss of subcutaneous fat. His cry was weak. On palpation of the abdomen peristaltic waves became visible, passing from left to right. No mass palpable. No distention or rigidity. Extremities showed considerable hypertonicity.

On admission to the Mount Sinai Hospital the child was put on breast feedings plus a whole milk mixture, and was given subcutaneous infusions of normal salt solution. One day after admission the child had a convulsive attack becoming alarmingly cyanotic. On the fourth day the weight had fallen from 7.9 to 7.3 pounds and atropin treatment was begun. At this time average breast feeding was 2 ounces, supplemented by 2 ounces of milk mixture. Bottle feedings were taken very reluctantly; the breast somewhat better. Vomiting after almost every feeding.

The subsequent progress of the case is shown in the accompanying summary. It will be noted that the atropin which was given by hypodermic injection was rapidly increased from 12 minims on June 29th to 49 minims on July 5th. This maximum dosage was maintained for six days, when it was gradually reduced, so that on July 17th the baby was taking but 1 drop by mouth with each feeding. On the atropin treatment it will be noted that the constipation was overcome, the vomiting became gradually less in amount, and then stopped altogether, and twenty-five days after admission in a seriously sick condition the baby was discharged well.

He was seen by me on July 22d, weighing 8 pounds, 7 ounces. On August 5th, 9 pounds, 5 ounces, and on September 8th (three and a half months old) weighing 12 pounds, 13 ounces.

Summary.—Case of pyloric stenosis with severe symptoms due to loss of fluid. Prompt recovery under atropin administration and subcutaneous introduction of fluid.

SUMMARY OF CASE I

Date	June					July.																
	26	27	28	29	30	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Breast milk, ounces	4	12	13	12	11	10	9	10	8	8	5	6	8	10	10	10	10	10	10	10	10	10
Formula, ounces	6	6	15	14	11	14	13	16	16	17½	17	17	18	16	18	20	17	17	18	18	18	19
Water, ounces	..	..	..	2	3½	2	2	1	2	..	6	..	..	..	2							
Subcutaneous infusion, ounces	9	13	13	..	..	..	5	5														
Vomitus, ounces	3	7	13	13	6	6	11	7	7	4	6	1	4	2	2	4	2	..	..	1½	1	
Stools, No.	..	2	..	..	2	2	1	1	1	2	1	1	2	2	3	1	2	3	1	2	2	2
Weight, pounds	7.5	7.9	7.4	7.3	6.15	6.14	6.14	7.5	7.1	7.3	7	7.2	7.3	7.3	7.7	7.10	7.10	7.12	7.13	7.14	7.14	7.15
Atropin solution, drops	..	..	..	12	15	18	21	31	36	49	49	49	49	49	49	42	35	28	21	14	14 (per os)	7

CASE II

Kenneth G. First seen when three and a half weeks old on May 11, 1920.

Family history negative.

Chief complaint, vomiting since ten days. Past history: Full-term, normal birth, breast fed to date, slight jaundice when three days old. Present illness: Projectile vomiting immediately after feeding or within an hour of it. Loose stools till four days ago, since which time child has been obstinately constipated. Peristaltic waves noted on the abdomen. Birth weight 8 pounds, 12 ounces. Weight on admission 8 pounds, 2 ounces.

Physical Examination (May 12, 1920).—On admission to Mount Sinai Hospital (Service of Dr. H. Heiman) fairly well-developed and nourished male infant. Moderately jaundiced. Except for abdominal findings, physical examination was negative. In the epigastric region a distinct wave could be seen, especially after feeding, starting below the left costal border and traveling downward and to the right. On deep palpation in the epigastric region below the right costal margin there could be felt a small nodule about the size of the tip of the little finger.

This infant was put on atropin by mouth, and the dose was slowly increased so that a maximum dosage of 10 drops of atropin solution was only reached after the child was in the hospital a month. The weight during this time fluctuated between 8 pounds and 8 pounds, 5 ounces. Vomiting was frequent, though stools became normal as soon as atropin was administered. On gradually increasing strength of evaporated milk and water solution the baby gained, so that on June 1st the weight had reached 9 pounds, 12 ounces. The atropin was stopped several times in this case to ascertain whether the drug was really influencing the illness. On each occasion of the withdrawal of the atropin the vomiting would increase, the stools would become fewer, and the infant would have periods of great restlessness and distress, often not sleeping for many hours at a time. On starting the atropin again the symptoms would be promptly relieved. After being in the hospital two and a half months

the infant contracted pertussis, and was taken home, where atropin was continued by mouth. The child made an excellent recovery, and when seen at the age of seven and a half months weighed 18 pounds, 1 ounce.

Summary.—A typical case of pyloric stenosis with visible wave and palpable tumor. Atropin administered irregularly and usually by mouth every three hours. After large doses were inaugurated gain in weight was more rapid—27 ounces in twenty-four days. Treatment interrupted by whooping-cough. Recovery.

CASE III

Bruce MacD. First seen May 12, 1921, at the age of two weeks.

Family history negative.

Second child; first child operated upon at the age of three weeks for pyloric stenosis.

Past History.—Normal delivery. Birth weight 7 pounds, 5 ounces. Breast fed to date every three hours. For the past two days has vomited large amounts after feeding. Vomiting distinctly projectile.

Physical Examination.—Showed a well-developed male infant with a marked peristaltic wave passing across the abdomen. After nursing, the entire feeding was almost immediately vomited, vomitus shooting out of the baby's mouth and nose.

An evaporated milk mixture was prescribed, but vomiting continued. A stomach-tube was passed immediately before a feeding and a large amount of milk was found retained in the stomach. On May 15th atropin was begun and continued as shown in accompanying chart. On May 15th a small abdominal mass was felt. May 19th child was seen by Dr. L. Holt, who corroborated the diagnosis. During the treatment the atropin was run up to 64 drops on May 30th, and then varied according to the symptoms. Various formulas, including evaporated milk, cereal, and breast milk, were offered. The vomiting, though severe in the beginning, gradually diminished and the stools became regular. The baby's weight, from 7 pounds, 2

SUMMARY OF CASE III

Date	May.																	
	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Food, ounces	12	8	11	9½	13	?	12	13	11	11	13	15	19	13	15	17	20	14
Water, per os	...	...	...	...	...	...	2	2	...	2								
Water subcutaneously	...	...	...	...	...	...	...	...	+									
Vomitus	++	...	2	3	2	+	5	5	2	2	2	4	3	1	2	1	2	3
Stools	...	1	3	4	...	...	2	...	...	7	1	...	...	1	1	1	1	2
Weight, pounds	7.2	7.2	7.4	7.4	7.1	7.1	7.1	7.2	7.5	7.3	7.2	7.5	7.6	7.5	7.7	7.5	7.8	7.9
Drops of atropin	12	12	18	22	30	25	38	39	42	48	48	42	54	48	53	59	64	56

Date	June.																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Food, ounces	17	14	14	16	15	11	18	17	17	9+	9	10	12	10	16	21	17	16	20	21	22	21
Water per os																						
Water subcutaneously																						
Vomitus	1	1	1	1	..	1	4	1	2	1	..	..	1	1	..	2	..	..	..	..	1	
Stools	1	1	1	..	2	6	..	1	1	1	1	1	1	1	1	7	1	1	1	1	2	2
Weight, pounds	7.8	7.8	7.7	7.10	7.9	7.9	7.11	7.13	7.10	7.14	7.14	7.15	7.15	7.14	7.15	8.3	8.5	8.5	8.7	8.10	8.10	8.12
Drops of atropin	64	56	32	56	32	40	48	48	49	54	54	45	45	35	41	40	22	28	17	16	16	10

ounces, dropped to 7 pounds, ½ ounce, and then slowly increased during the month of treatment, so that on June 14th the baby weighed 7 pounds, 14 ounces. From then onward the gains were much more rapid (12 ounces a week), so that the atropin could be rapidly diminished. On June 23d, six weeks after starting treatment, the infant was sent to the country, with instructions to use small doses of the atropin by mouth.

One year later the parents reported that the child was in perfect condition and had remained entirely cured.

Summary.—A severe case of pyloric stenosis in a breast-fed infant showing visible peristalsis and palpable abdominal tumor. Large doses of atropin were necessary. Weight slowly increased during the first month of treatment, then very rapidly. Complete recovery. Second child, having had similar illness, was treated by operation.

CASE IV

Jack P. First seen May 2, 1921.

Family history negative.

Second child, normal birth, two weeks old, breast fed. For two days child has vomited immediately after nursing. Stools constipated. No other symptoms. Birth weight 7 pounds, 6 ounces.

Physical Examination.—Showed a baby with evidence of recent loss of weight. A slight peristaltic wave was visible, which after several days became very marked. No palpable tumor felt. On being fed the baby vomited practically the entire feeding in a very forcible projectile manner. Atropin was begun on May 2d, when the baby was three weeks old, and continued for four weeks. The largest daily dose found necessary was 40 drops of the 1 : 1000 solution. The evidence of dehydration necessitated administration of water, which was given in the form of Murphy drip. The accompanying table shows the progress of the case. After four weeks of treatment the baby's weight had risen from 6 pounds, 9 ounces to 7 pounds, 15 ounces. It will be noted that in the middle of the second week of treatment, when the dose of atropin had been increased to 40 drops,

SUMMARY OF CASE IV

Date	May.																												
	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Breast milk, ounces..	..	7	11	13	15	16	11	14	14	10	21	15	19	16	13	12	20	12	7	8	7	7	4	3	3			
Formula, ounces....	14	4	..	..	..	½	8	3	3	5	..	5	4	9	12	8	12	16	23	25	17	19	18	22	21	27	24	26
Water, Murphy drip	3	19	7	4	5	11	3	3	4	2	2	3	3															
Water per os.....	..	..	..	..	..	..	1	½	..	..	..	..	..	1	1	1	1											
Vomitus.....	4	2	2	1	2	2	2	3	2	3	..	3	1	..	..	1	1	..	1	1	1	1	1	2	1	1	..	1
Stools.....	2	1	5	2	1	3	1	2	2	1	2	4	3	2	2	4	2	2	2	2	5	2	1	2	3	1	2	3
Weight pounds.....	6.9	6.9	6.11	6.13	7	7	..	7.8	7	6.14	6.15	7.1	7.2	7.2	7.6	7.6	7.6	7.7	7.7	7.8	7.8	7.9	7.10	7.11	7.12	7.13	7.14	7.15
Drops of atropin....	9	20	25	33	34	32	28	32	32	35	40	42	27	25	40	35	40	40	40	30	15	20	15	10	20	15	20	15

the first twenty-four-hour period free from vomiting occurred. After the fourth week of treatment the atropin was rapidly diminished and the gain was uninterrupted. At the time of writing the baby is a perfectly normal child.

Summary.—A severe case of pyloric stenosis showing projectile vomiting and visible peristalsis, but no palpable tumor. Marked evidence of water loss. Atropin administered up to 40 drops of 1 : 1000 solution a day. Complete recovery in four weeks.

CLINIC OF DR. JESSE G. M. BULLOWA

WILLARD PARKER HOSPITAL

POSTPNEUMONIC OSTEOMYELITIS OF THE PUBIC BONE

INFLAMMATORY disease of the pelvic bones is not common, and when they are involved the pubis is affected in only 6 per cent. of the cases. I have been able to collect only 40 cases of pubic osteomyelitis from the literature. Most of these have been reported from France. Most have proved tuberculous and have occurred in adolescents. One case resulted from the trauma of delivery. Osteomyelitis as a sequel of pneumonia is rare and is unmentioned in most text-books.

The present case is especially interesting because of the mature age of the patient and the apparent etiology. I am fortunate in being able to report this interesting case through the courtesy of Dr. William B. Giles, with whom I saw him in consultation.

H. D., a merchant fifty-nine years of age, was in good health until May 7, 1922, when he was taken with chilly sensations and diarrhea. His temperature rose to 100.8° F. His pulse was 96 per minute. His lungs were apparently clear until the following day, when râles were found in the right lower lobe. Later the middle lobe was involved, and in the second week the lower lobe of the left lung was consolidated. The temperature varied between 102° and 104.6° F., the pulse between 130 and 140 per minute. The sputum was abundant and bloody. After the fifth day the pulse was extremely irregular.

From the sixth to the twelfth day the patient was delirious and has no recollection of what transpired. The delirium was active with attempts to leave his bed, frequently requiring restraint. He did not respond to the usual mild sedatives and

hypnotics, and it was thought unwise to depress him with those more powerful. On the eighth day marked cyanosis developed, with evidences of pulmonary edema, which lasted eighteen hours and which seemed to clear after an intravenous injection of guaiacol and iodin, given as a last resort by Dr. Giles. On the tenth day there was a brief collapse, from which the patient reacted after a subcutaneous injection of camphor in oil. On the fourteenth day the mental condition was normal, the heart was regular, the temperature 100° F. The patient sat up out of bed on the fifteenth day. The sputum showed pneumococci and no tubercle bacilli on several occasions. The Wassermann was negative and the blood-pressure was systolic 160, diastolic 90. The urine was free from albumin and sugar.

The patient attributes his present illness to overzeal on the part of his nurses in restraining him. He was first seen in consultation on October 12th, and complained of tenderness over the pubis, which had lasted three weeks and was steadily increasing. There was distress on walking, in lying prone, and in climbing stairs. There were no sleep-starts. The pain is referred chiefly to the inner surface of the thigh, especially the left. All movements of flexion, extension, and abduction at the hip are painful. The patient is most comfortable with a low-back rest and with the thighs semiflexed and the knees supported.

On examination, there is a fulness of the symphysis pubis, with marked tenderness over the bodies of both pubic bones and rami. Pain is referred to the symphysis on crowding the ilia together. A rectal examination reveals a uniformly large prostate. It was impossible to reach the posterior surface of the pubis to elicit tenderness. There was no abscess. It is quite evident that the movements which are painful are those involving muscles attached to the pubis, the pectineus, the rectus abdominis, the adductor longus and brevis, and the gracilis. Movements of the trunk involving balancing of the pelvis are painful. Movements of the thighs, with the pelvis as a fixed point, cause distress.

The radiograph is especially instructive and helpful in diagnosis. There is rarefaction of the body of the left pubic bone

and a mouse-eaten appearance of the mesial cephalic portion of the bodies of both pubic bones involving the joint. There is increased density about the most markedly rarefied portion. There is no periosteal involvement.

The lesion is solitary and involves the homologue of a long bone shaft, and has commenced in the medullary portion. All these facts are, moreover, indicative of an inflammation in bone

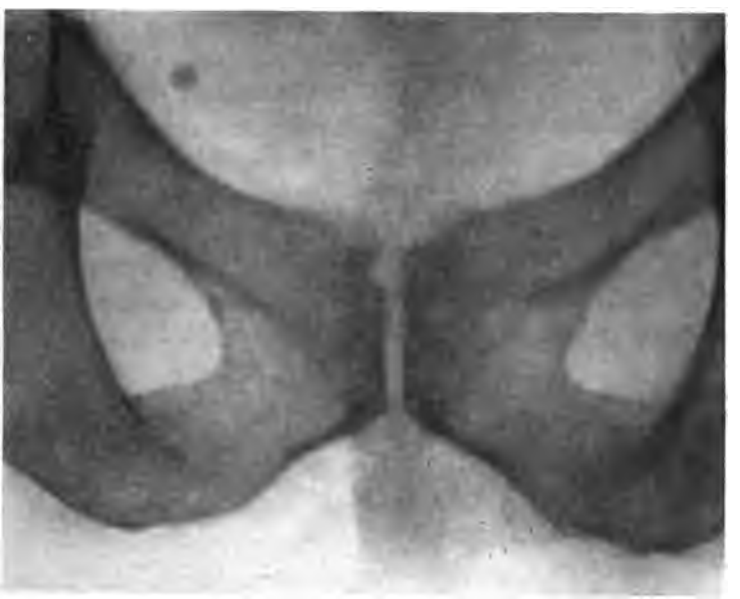

Fig. 112.—Postpneumonic osteomyelitis of body of the pubic bone. Rarefaction of body most marked on left side. Mouse-eaten appearance of bone involving joint. Note also increased density about rarefaction zone and absence of periosteal proliferation. The lesion is solitary.

due to pyococci. It is the habit of pus-forming organisms to produce this type of inflammation and elect this site for their activities. It is probable that the organisms were carried to this location by the blood-stream while it was infected during the pneumonia. The situation may have been determined by the necessary zeal in restraint.

A syphilitic lesion would have been characterized by mul-

tiple foci which show proliferation, especially of the periosteum. It rarely involves the joint and diaphysis.

Tuberculosis, though usually solitary and destructive, does not, as a rule, show any regeneration of bone, and is usually primary in the epiphyseal portion of a bone.

Paget's disease is a proliferative process. Periosteal sarcoma is of the same nature, while medullary sarcoma is purely destructive, as is also giant-cell sarcoma. Bone cysts are also purely destructive and spare the joints.

The *x*-ray evidence in conjunction with the history and physical signs apparently justify the diagnosis of a postpneumonic osteomyelitis involving the body of the pubic bones.

The patient has been made comfortable in a sitting position in a Morris chair for four weeks. Stock pneumococcus vaccine has been administered in increasing doses. There have been severe local, but no focal reactions. The patient has improved considerably. The edema and swelling about the pubis has disappeared and the pain has become much less severe.

THE "SIXTY-SIX" PULSE

EVER since the introduction of instruments of precision (and watches ought certainly to be so regarded) numeric standards for physiologic relations have been possible in medicine. Certain numeric constants are frequently involved in our interpretation of symptoms, and they must be promptly recognized. To catalog and explain all the numeric values which as physicians we keep in mind would require more space than this clinic would allow. Variations in the numeric values for the circulation are those most frequently encountered.

The usual pulse-rate for adults is given as 72 per minute. Of course this is only the mode, and the extremes are from 70 to 76 per minute. Because the usual practice is to count one-quarter to one-half minute, an even number is found. If pulses are charted as ordinates the steps are usually in pairs of beats per minute for ease of reading, and this probably accounts in part for the frequency with which an even numbered constant has been found under certain conditions. Attention is more certainly arrested by large variations, especially when the rate is increased. This is probably due to the fact that such accelerations of rate usually accompany temperature rise and are frequently present during acute or chronic menacing situations. Slowing of the pulse is not as noticeable when charted, and the important figure which I wish to emphasize is only 8 per cent. below the average, a reduction of one-twelfth. Moreover, in acute conditions it is usually of very brief duration, and has given way to acceleration of 30 or 40 per cent. by the time patients reach the hospitals, and are seen by consultants, internes, and students.

The most marked slowing of the pulse seen only in total heart-block when the ventricle assumes its own rate of 28 to 32 per minute is rarely seen, and then it is only a 60 per cent. reduction from the average normal pulse-rate. However, this

is a reduction of more than one-half the normal rate. Pulse-rates of 120 to 140 are common and represent almost a 100 per cent. increase.

The importance of the 66 per minute pulse-rate is stressed because it is an objective sign of pain. With rise of blood-pressure it is a measure of intense painful afferent impulses which may be valued regardless of an individual's habit of exaggeration. The 66 per minute pulse-rate in acute conditions is a physical sign of vagotonia which cannot be disregarded with impunity. It is evidence either of an overacting vagus or of a deficient sympathetic innervation of the heart. Recent experiments by Hamburger, of Groeningen, Holland, show that metabolites from stimulated organs may account for the frequency of vagotonia in acute abdominal conditions. Hamburger discovered that the venous blood from a vagus stimulated organ would produce the vagus action when perfused through the organs of another animal. The 66 pulse as evidence of vagus tone is an important and often disregarded sign of the severity of irritative abdominal lesions, as the following case exemplifies:

An adult male ten years after his typhoid fever was subject to mild attacks of right upper quadrant pain. A final attack, more severe than those preceding, was associated with a pulse of 64, rectal temperature of 98° F., and slight nausea. Eight hours later the right upper rectus was rigid; the temperature 99° F., and the pulse 80. In spite of the toxic appearance of the patient the attending physician refused, because the pulse was slow and the temperature low, surgical consultation until the following morning; then the pulse had risen to 114 per minute and the temperature to 101° F. Two hours later laparotomy revealed a gangrenous gall-bladder with free fluid in the peritoneal cavity. Convalescence was lengthened by the necessary drainage and the surgical risk was definitely increased.

Two other cases illustrate the importance of slow pulse in acute abdominal conditions.

A young man of twenty-four had so frequently complained of vague fleeting abdominal pains that his family regarded him

as a neurotic, eager for sympathy. The tentative diagnosis of chronic appendicitis had been made on point tenderness and hyperalgesia; but these were not constant; operation was deferred. The usual pulse-rate was 74. After a customary Sunday evening cold meal there were severe abdominal cramps, nausea, and belching. Of course the meal was blamed. When seen two hours after the onset the pulse was 66 per minute, rectal temperature 98° F. There was hyperalgesia of the eleventh dorsal segment, Meltzer's sign was present, but not decisive. The abdomen was rigid. Pain was referred to the epigastrium. Gas did not pass with enemas. Two hours later the pulse was 72 per minute, without abatement of the symptoms. The temperature did not rise. After another two hours the patient vomited; the pain came in attacks, about fifteen minutes apart, and was cramp-like in character. The distress had now shifted to the right lower quadrant. The Meltzer sign was definite. Gas had been passed with repeated enemas. The pulse was 80 per minute, the temperature 99.2° F. by rectum. The white blood-count was 11,000, polynuclears 78 per cent. Three hours afterward the abdomen was opened and an appendix swollen to the size of the index-finger was found coiled in the ileocecal fossa, with its base constricted by a band of peritoneum. Convalescence was eventless. The abdominal symptoms have cleared away.

K. D. is a lawyer. He had served in the trenches in spite of a healed pulmonary tuberculosis. He had been under observation for a suppurative cervical adenitis, which had healed. The usual pulse-rate was 74 per minute. There had been no previous abdominal symptoms other than an attack of severe painful diarrhea while in France, two and one-half years before. Without previous distress or symptoms, he was seized, while in his office, with severe abdominal pain which was unlocalized. Without advice the patient took a bottle of citrate of magnesia. He was seen two hours later in my office. The abdomen was scaphoid. There was marked complaint of pain referred to the umbilical region. There was no tenderness. The pain was constant. The pulse was 66 per minute, rectal temperature

98.8° F. There was marked pallor. The blood-pressure was systolic 150, diastolic 90. On previous occasions the figures had been systolic 120, diastolic 70. There was no nausea; gas had been passed. There were no exacerbations of the pain and the pain was not relieved by morphin. Ten hours later the pulse-rate was 78 per minute and the temperature 99° F. The pain was still intense. There were no localizing symptoms. Sixteen hours after the onset the pain had been only slightly relieved by ¼ grain of morphin. The patient was nauseated and there were now exacerbations of distress. The pulse was 80 per minute, the temperature 99.6° F. Flatus was not passed. An enema was ineffectual. There was no Meltzer sign. Intestinal obstruction and acute appendicitis were discussed and the performance of a laparotomy decided upon. At the hospital the blood-count was 12,000 with 80 per cent. polynuclears. Before operation the temperature had reached 100.6° F. and the pulse was 90. The laparotomy revealed a strangulation of a loop of ileum, behind a band running from the tip of a Meckel's diverticulum to the ileum. There was no free fluid and the gut was almost normal in appearance before the abdomen was closed. The patient was up and about in ten days. All these cases showed an initial "66" pulse.

The intestinal tract is not, however, the sole source of such vagotonic slowing of the pulse-rate.

H. S., fifty-two years of age, was awakened with severe right-sided lumbar pain. There was urgency and frequency of urination. A self-administered cathartic caused free movement of the bowels, but afforded no relief from the pain. Ten hours later the pulse was 66 per minute, rectal temperature 99.6° F., blood-pressure systolic 210, diastolic 100. The usual pulse-rate is 76 per minute and the blood-pressure systolic 180, diastolic 90. The urine contained many red blood-cells. There was no rigidity and no hyperalgesia. The course of the right ureter was tender. Benzyl benzoate relieved the pain in one-half hour and it has not recurred.

There are two other occasions when the 66 per minute pulse-rate proves of interest. During the administration of digitalis,

before nausea or coupled beats appear, the evidence of ample vagus stimulation from the drug may be the 66 per minute pulse. In diphtheria the sympathetic system is at first stimulated by the toxin. Acceleration of the pulse-rate is a characteristic symptom. The toxin is, however, a specific poison for the sympathetic nerves. During convalescence, as the pulse-rate returns to normal, in over three-quarters of the cases there is a drop below the normal, usually to 66 per minute, before the normal 72 per minute rate is resumed. This evidence of sympathetic intoxication may be transitory, or it may presage a greater and later drop to 40 per minute or thereabouts, a bradycardia from cardiac muscle involvement.

Slowing of the pulse to 66 per minute results from vagus stimulation and occurs in acute painful abdominal disease, as the result of ample digitalis action, and when the vagus is unopposed from depression of the sympathetic in diphtheria.

CONTRIBUTION BY HERMAN O. MOSENTHAL

POST-GRADUATE HOSPITAL

MAINTENANCE BY DIET IN THE TREATMENT OF DIABETES MELLITUS[1]

TWENTY years ago diabetes mellitus was treated by the elimination of starchy foods from the diet and by curtailment of proteins, whereas fats were allowed in abundance. The result was that the cases which progressed died in coma. Subsequently Frederick Allen demonstrated that food restriction could be carried out much more rigidly, without producing a dangerous degree of acidosis, provided the intake of fats was properly regulated. More recently Schaffer and Woodyatt have elaborated formulæ by which, if it is known what food substances are utilized within the body, an accurate estimate of the degree of acidosis to be expected may be obtained.

A mastery of these comparatively simple principles has made it possible to achieve a sugar-free urine, a normal blood-sugar, and freedom from acidosis in many instances where this was considered to be impossible before. There is no doubt that if these criteria of successful management of the starch metabolism in any case are kept up, the best chances of increasing the carbohydrate tolerance of the patient are present and the possibility of the disease progressing is reduced to a mimimum, though it is not set aside. If the power of the body to utilize glucose does diminish, the plane of nutrition must be adjusted to a lower level to meet this emergency. As the disease advances and the

[1] This contribution was presented before the use of pancreatic extract for the treatment of diabetes mellitus was made possible. It is believed, however, that the facts discussed in this clinic are of importance and will continue to be so even if the newer method of handling this disease will change the therapeutic aspect of diabetes a great deal.

diet is curtailed so as to meet the demands of the most effective therapy, that is, a sugar-free urine and a normal blood-sugar level, a time comes when there is not sufficient nourishment provided to maintain health and strength and the dangers of inanition must be considered. The physician is then confronted with the dilemma of starving his patient unduly or not enough.

The following are examples of this possibility:

A child aged seven had for one year and nine months been kept sugar free and had a persistently recurring hyperglycemia held in check by means of very drastic food regulation; the carbohydrate tolerance had diminished to such a degree that there was an excess of sugar in the blood on a diet containing 30 gm. of protein, 15 gm. of carbohydrate, and 80 gm. of fat; the child was pale, thin, fatigued easily, and weighed but 37 pounds; it had been definitely established that the diabetes in this case had progressed in spite of the most rigid dietary restrictions and that death from malnutrition was imminent.

A man aged forty-two has been suffering with diabetes for one year; during this period the disease has been properly controlled by diet; in spite of this the severity of the condition has progressed until now the urine can only be kept free from glucose by starvation; he has lost 40 pounds, his weight is reduced to 110 pounds, and he is extremely weak.

Another instance is that of a girl aged seventeen, who had had diabetes for seven years; her weight was reduced to 65 pounds; by dietetic restriction the urinary glucose had been held in check; at this time she showed traces of sugar on a diet of 375 calories, and her father wrote "unless we can give some increase in diet, I do not see how she can survive much longer."

These cases represent the rather large class of diabetics that nearly every one has come in contact with. From the clinical point of view the diabetic symptoms are under control, but the patient is approaching the limits of endurance because of lack of food; under these circumstances the disease is being treated, but the person suffering with it is not. Here two modes of procedure present themselves: Either the criteria of successful control of the carbohydrate metabolism shall be striven for and

nutrition disregarded, or a moderate diet be ordered that furnishes some nourishment while glycosuria and hyperglycemia exist. In either event the prognosis is exceedingly gloomy; if the former method is pursued the patient will have his carbohydrate metabolism properly controlled; if the latter scheme is adhered to he will live more comfortably and often exhibit a surprising amount of vitality.

It must be understood that all dietary restrictions are never to be cast aside. This is attended by disastrous consequences. The history of one man aged thirty-nine in this connection may be regarded as typical. This patient's sugar tolerance had been progressively diminishing; he realized the gravity of the situation and made up his mind to take matters into his own hands; he left New York for a hunting trip in the Canadian woods, paying no attention whatsoever to his diet; he returned in a few days suffering with an agonizing thirst and a polyuria that allowed no rest during the day or night. From a small volume of urine and a slight degree of glycosuria a state had been reached in which this man excreted 10 liters of urine and 500 grams of sugar a day. Such extremes in diet should not be countenanced, and complications of this sort are not brought about if these patients are given only a moderate amount of food that is commensurate to a certain extent, at least, with their needs.

As an example of the successful application of these ideas the following case may be cited: This is the man forty-two years old, weighing 110 pounds, already referred to; he could eat virtually no food without exhibiting glycosuria and was so weak that he was in bed a great part of the day. He was given a diet of about 1500 calories; the proportion of fat, proteins, and carbohydrates have been varied from time to time so as to control glycosuria and acidosis as much as possible. For a period of six months this man has possessed enough vitality to do a full day's work and to feel comparatively well and strong. Even if nothing more should be accomplished these added six months of physical well being are worth while. His urine during this time contains about 50 grams of glucose and the blood-sugar

is at a level of about 0.285 per cent. In treating these cases the physician must have a definite policy in mind, either longevity must be aimed at by maintaining the blood and urinary sugar at a normal level by means of undernutrition, or a moderate amount of food can be administered giving the diabetic a little more comfort, a greater vitality, and not necessarily curtailing his span of life, in fact, sometimes prolonging it. Personally I have always preferred the latter alternative, and with added experience feel that I am justified in this belief. In adult patients the wishes of the diabetic himself in regard to the mode of treatment to be followed may be consulted.

If the end-picture in diabetes presents the dual and irreconcilable problem of the necessity of food assimilation, on the one hand, and the demand for a sugar-free urine on the other, cannot steps be taken early in the disease to forestall the urgency of this situation? This can be accomplished by the physician who guides the initial treatment. With the great publicity that has been accorded the subject of glycosuria and prophylactic urinary examinations, patients suffering with diabetes mellitus usually present themselves for very early diagnosis and treatment. Such cases should be handled with all possible care. It has been the custom of some clinicians to starve these cases immediately or after a short period of a fat-free diet. By these means the carbohydrate metabolism is controlled effectively and in the briefest possible time. Under this régime much body tissue is lost; sometimes this is so great as to become alarming. It should be remembered that medicine teaches that diabetes may be controlled, but not that it can be cured. Consequently the time element within a limit of days plays no part in the management of this malady. If there is no object in speed of desugarization is there any inherent quality in drastic undernutrition that render its employment imperative in every case?

A complete desugarization may be accomplished in most instances of diabetes without having recourse to starvation. Of the cases recently treated, excluding those seen only a few times, the very mild cases, those already sugar free and those who did not co-operate, there were:

18 desugarized on a protein fat diet taken as desired.
8 desugarized on a protein fat diet of 1000 to 1500 calories.
3 desugarized on a protein fat diet of 500 to 1000 calories.
4 desugarized by starvation.

By "desugarization" is meant the elimination of sugar from the urine and the reduction of the blood-glucose to normal. Even if this number of cases is small it is clear that in many diabetics it is possible to control the digestion of starches without resorting to more than mild dietary restrictions; the same is true in regard to special attention to acidosis, though this factor should never be lost sight of. Under this dietary scheme the patients are kept upon an unrestricted protein fat diet or upon a 1500-calorie diet of protein and fat until the sugar in the urine ceases to diminish. If it does not entirely disappear, then progressively increased food restrictions are ordered until the process of desugarization is complete. There are some very distinct advantages in this slower and more conservative procedure. The most important of these is that the nutrition, health, and strength of the patient are conserved as far as possible; by these means a certain reserve is provided in case the disease becomes unmanageable and more vigorous food restrictions prove to be necessary. It must be realized in this connection that in diabetes it is always an easy task to make the patient lose tissue, but it is often impossible to accomplish the opposite and restore health, strength, and nutrition. It is an urgent necessity, therefore, to proceed conservatively especially during the first period of treatment; mistakes due to overcaution in undernutrition may be corrected, while the overenthusiastic use of starvation may result in a state that cannot be rectified, and that could have been, in part at least, prevented.

The importance of maintenance in diabetes in the initial and terminal stages of the disease has been discussed. This leaves the comparatively long intermediate period when the disease improves, remains unchanged, becomes more severe, or shows a bewildering variation of these three possibilities. There is no condition in which the individual peculiarities of the patient have to be taken into consideration more than they do in

diabetes. Two extremes may be cited to show how wide a variance may occur. A member of the Officers' Training Corps was brought into a base hospital and in less than two days died of diabetic coma; investigation disclosed that he had passed several physical examinations, including urinary analyses, a short time previously, and nothing abnormal had been discovered; his room-mate noted that two weeks before his death sudden intense thirst and polyuria had set in; this may be considered to be a case of acute fatal diabetes mellitus of only a few days' duration. This history is in marked contrast with that of a man forty-eight years old, who was rejected on life insurance examination ten years previously because of the presence of albumin and sugar in the urine. The medical examiner met him a year later and is reported to have involuntarily exclaimed: "Man, are you still alive?" This spurred the diabetic to action, and on the advice of a friend he treated his albuminuria by a low protein diet which he has continued since that time. The diet is worth considering:

Breakfast: 2 glasses of milk.
Lunch: 2 eggs, 4 to 6 rolls, butter.
Dinner: Clear soup, meat about 8 ounces, vegetables, potatoes, ¾ loaf of bread, butter, fruit.
10 P. M.: Glass of milk.
For four years much beer was indulged in; for the last six years none was taken.

It is scarcely credible that this man should live ten years after breaking every rule that was ever formulated for the care of diabetes. However, he had lost no weight, in fact, was obese, weighing 225¼ pounds, the height being 5 feet, 8½ inches; there were no signs or symptoms giving any evidence of endocrine disturbance; there were only two signs or symptoms, besides a very marked glycosuria, that could be referred to the diabetes, these were impotence and absent knee-jerks.

Thus far no noteworthy attempt has been made to differentiate the benign or stationary from the malignant or progressive type of diabetes. In a general way it is known that children exhibit the severest form of the disease, but even here excep-

tions occur. Why does one case progress rapidly while the other does not? The answer of this question is probably to be found in the cause of diabetes. It is realized that changes in the islands of Langerhans in the pancreas bring about a diminished ability to utilize starches, but what factors, in turn, are responsible for such pathologic lesions? Infections even of slight degree may often cause an exacerbation of an existing diabetes, therefore it may be assumed that the absorption of toxic material from an infective focus may be to blame in some cases; the blocking of the common bile-duct and forcing of bile into the pancreas is another recognized cause; pancreatic calculi may be responsible in some cases; arteriosclerosis of the pancreatic vessels undoubtedly results in some of the slowly advancing types in elderly individuals; in the main, however, there is little known concerning the cause of the pancreatic lesions. If this knowledge were at hand some cases might be cured.

If there are multiple causes for the changes in the islands of Langerhans, some of which are presumably active for only a short period, while others are constantly bringing about further pancreatic damage, then there must be some instances in which there is acute disease which subsequently does not progress, whereas others must exist in which the constant deterioration of the pancreatic tissue is distinctly evident.

It would be a very great advantage if these clinical types could be distinguished one from the other. At present the attempt is made to treat them all alike. No one treats all cases of pulmonary tuberculosis, whether they are active or inactive, in precisely the same way. However, that is to a great extent the scheme of dietetic therapy that is being accorded the individual that is suffering with diabetes mellitus. The past history of any case furnishes a distinct clue as to how rapidly the condition has advanced; the disease, as is well known, is more prone to be severe in the young than in the old; nervous alert individuals are more subject to exacerbations than those with a placid disposition, obese diabetics are often found to progress very slowly; there are many exceptions to the above statements, but they and many other facts that will have to be

developed by further observation serve to point out the way for the most suitable dietetic therapy.

If maintenance cannot be accomplished by a diet that brings about a sugar-free urine and a normal blood-sugar, and the patient is losing an undue amount of flesh, strength, and vitality, it is well worth while considering the possibility of increasing the food at the risk of overstepping the conventional criteria of blood and urinary sugar with the idea that in some instances the progress of the diabetes is not accelerated, but even checked, and the nutrition of the patient benefited. Such steps should be taken with due caution, and are to be regarded as an experiment, much as any dietary change in diabetes, and the patient watched closely from day to day. If the trial is not a success, this can soon be determined, and the necessary measures taken to correct any harm that may have been done. A few examples of such dietary procedures are as follows:

A woman aged fifty entered the hospital suffering with marked furunculosis and great weakness; it seemed at the time that her outlook was very serious unless she could assimilate food and grow stronger; accordingly she was given a diet of 700 calories, although the fasting blood-sugar was at a level of 0.20 per cent.; in a week the blood-sugar had dropped to 0.17 per cent.; the diet was then increased to 1000 calories; at the end of another week the blood-sugar remained virtually unchanged when the food intake was increased to 1250 and later to 1500 calories; the patient did well, the furunculosis improved considerably, and she was able to take care of herself, a picture which was in marked contrast to the bed-ridden patient who had been shifted into the hospital as a last resort to save life. If the diet had been so low as to produce a normal blood-sugar this individual would, in all probability, not have survived.

A man was first seen in November, 1913; he was then forty-two years old; he had suffered with diabetes for eight years at that time; his urine contained 2.6 per cent. of glucose; he consistently indulges in more food than he should and glycosuria has been absent on only two occasions, once in 1920 and again in August, 1921; his weight has increased in nine years from

143 to 161 pounds and physically he feels well. There is a distinct possibility in this case that by maintaining his nutrition he has lived longer than if he had established a sugar-free urine at the expense of his body tissues.

In many patients above sixty traces of glycosuria are not accompanied by progressive loss of sugar tolerance.

A man aged fifty-nine has had diabetes for eleven years; he does not feel up to the mark physically unless he eats a considerable amount of food; consequently he insists upon rather a high diet that keeps his blood-sugar in the neighborhood of 0.200 per cent.; for four years the glycemia has been at about this level without causing apparent harm; a lower diet, while rectifying the glucose level in the blood, would have put the patient distinctly below par from the physical point of view.

Marsh, Newburgh, and Holly[1] have recently shown that nitrogen equilibrium could be maintained on a very low protein, low starch diet when enough calories were provided in fat. The same diets, but of lower caloric value, were used to desugarize diabetics (Table I). It was claimed, and I have found this to be true in occasional instances (see Table II), that the patient's urine could be rendered sugar free on this diet when starvation had failed. The large quantity of fat offered serves to diminish the amount of the body's protein that is destroyed on this diet as compared to starvation and, therefore, the protein-sparing effect of the fat not only brings about a lower level of sugar metabolism (60 per cent. of protein metabolized is changed to sugar) but also lessens the inanition attendant on starvation.

TABLE I

APPROXIMATE FOOD VALUES IN THE DIETS OF NEWBURGH AND MARSH[2]

Diet.	Protein, gm.	Fat, gm.	Carbohydrate, gm.
No. 1	20	85	15
No. 2	30	140	20
No. 3	35	170	30

[1] Marsh, P. L., Newburgh, L. H., and Holly, L. E., Archives of Internal Medicine, 1922, xxix, 97.

[2] Newburgh, L. H., and Marsh, P. L., Archives of Internal Medicine 1920, xxvi, 647.

In severe cases it seems doubtful whether the maintenance obtained by these means has very many advantages. Table II gives the extracts from the data of a boy in whom this diet attained its object in part, the urine was rendered sugar free, and a nitrogen balance was obtained; the blood-sugar never became normal. During the twenty-seven days, before a nitrogen balance resulted, there was a loss of body nitrogen; 146.2 gm. were passed in the urine in excess over the intake; allowing the conservative estimate of 13.8 gm. of nitrogen in the stools during this period, a loss of 160 gm. of nitrogen equivalent to 1000 gm. of protein is established during twenty-seven days. This is ā large amount, especially as during the previous starvation treatment there undoubtedly had been a large loss of nitrogen.

TABLE II

Date.	Urine.			Food.				Remarks.
	Glucose, gm.	Diacetic acid.	Nitrogen, gm.	Nitrogen, gm.	Protein, gm.	Fat, gm.	Carbohydrate, gm.	
								Starved for several three-day periods and not rendered sugar free.
May: 1	54	++++	11.8	3.2	20	89	15	Third day of diet.
5	56	++++	15.7	3.2	20	89	15	Seventh day of diet. Glycosuria largely due to destruction of body protein as evidenced by large amount of nitrogen in urine. Blood CO_2 23.8, indicating marked acidosis.
28	9	++	2.1	3.2	20	89	15	Thirtieth day of diet. Nitrogen balance obtained on twenty-eighth day. No acidosis. Blood CO_2 55.7; has been receiving bicarbonate of soda.
June: 3	0	0	3.8	3.2	20	89	15	Thirty-sixth day of diet. First day sugar free.

Extracts from the data of a case of diabetes mellitus, a boy weighing 75 pounds. The high fat, low carbohydrate, and protein diet required twenty-eight days before a nitrogen balance was obtained; during this period 160 gm. of nitrogen equalling 1000 gm. of protein were lost to the body; it required thirty-six days to bring about a sugar-free urine; a normal blood-sugar was not brought about, although the diet was continued for a total of ninety-eight days.

In the patients suffering with advanced diabetes I have not found this diet to be more than a temporary aid when it succeeded in rendering the urine sugar free. However, this often furnishes a welcome respite. As the disease progresses and the sugar tolerance diminishes the high fat content of the diet

results in acidosis which often terminates in coma unless the proportion of proteins, fats, and carbohydrates is changed. The case detailed above died in diabetic coma a few months later.

In the less severe cases the diet of Newburgh and his collaborators maintains the disease in apparent equilibrium very well. However, I am of the opinion that those diabetics to whom I have prescribed a higher protein intake than $\frac{1}{2}$ gram per kilo have done better, exhibited more vitality, than those kept on a minimum nitrogen intake. This can be a question of impressions only, as there is no actual method of proving this point. Rubner[1] apparently drew the same conclusion from his war-time observations.

Mosenthal and Harrop[2] showed some time ago that in the average diabetic protein in the food results in the assimilation of considerable amounts of nitrogen, while fat and alcohol do not. This work was criticized by Marsh, Newburgh, and Holly partly on the ground that the nitrogen was not determined in the feces. As a matter of fact, this chemical procedure was carried out, and it was so stated in the original article. Since that time the work of Rubner, quoted previously, and that of Hoesslin[3] and Kohn[4] amply bear out the statement made that in the diabetic or undernourished individual the retention of huge quantities of nitrogen is favored remarkably by protein food and much less effectively by carbohydrate, fat, or alcohol.

What becomes of this retained nitrogen has been debated for some time. It would lead us too far afield to take up this problem in detail. I should only like to repeat that it appears to me that the average diabetic patient feels stronger and more energetic if he can tolerate an intake of 80 to 120 gm. of protein than a bare maintenance quota of 40 gm. There is the objection of the increased metabolism evoked by the high specific dynamic action of the proteins and their high carbohydrate yield. These are to be considered and given their due in formulat-

[1] Rubner, Halbmonatschr. f. soz. Hyg., 1918, xxvi, No. 4.

[2] Mosenthal, H. O., and Harrop, G. A., Archives of Internal Medicine, 1918, xxii, 750.

[3] Hoesslin, H., Arch. f. Hyg., 1919, lxxxviii, 147.

[4] Kohn, Klara, Wien. klin. Woch., 1919, xxii, 135.

ing the diet in any patient, but when the diabetic's tolerance permits it the high protein ration will yield the best results as regards maintenance. A high protein or a high fat, low protein diet all have their indications and should be adjusted to the individual patient.

Undernutrition and maintenance by diet each play a distinct part in the successful management of diabetes mellitus. The best therapeutic results cannot be obtained if either one of these factors is slighted. The facts as given above are intended to show that the nutrition of the patient should be striven for throughout the entire course of the malady, and that in many instances it is often distinctly indicated to nourish the patient even though glycosuria and hyperglycemia are present.

CLINIC OF DR. ERNST P. BOAS

MONTEFIORE HOSPITAL FOR CHRONIC DISEASES

DISEASES OF THE AORTA AND AORTIC VALVES

LESIONS of the aorta and of its valves are always of interest to clinicians not alone because of the accuracy with which the diagnosis can usually be made but also because of the striking and dramatic character of the symptoms that accompany them. Moreover, within the last fifteen years the frequency and importance of syphilitic aortitis has been appreciated and its diagnosis rendered easier through the aid of the *x*-ray and the Wassermann reaction. As all diseases have their waves of popularity after attention has been drawn to them, so the term "aortitis" has become a commonplace in medical diagnosis, but, unfortunately, is being used quite uncritically, often with complete disregard of the underlying pathologic condition. It is not mere academic quibbling to demand that the term "aortitis" be restricted to such conditions in which there is an actual inflammatory process in the aorta. I shall discuss in this clinic the various processes that may affect the aorta, and point out which of these may properly be called by the name "aortitis."

About one-quarter of all patients with endocarditis present lesions of the aortic valves. Of 1914 cases of valvular disease at the Edinburgh Infirmary, 21.5 per cent. had aortic insufficiency alone, and 19.2 per cent. had aortic insufficiency associated with mitral disease. In my series of 536 cases (Table I) there were 6.3 per cent. with aortic involvement alone and 20.9 per cent. with combined aortic and mitral lesions.

Lesions of the aorta and of the aortic valves may be induced by a number of different agents. In making the diagnosis in a

patient with evident disease of the aorta and of the semilunar valves it is not sufficient to note the anatomic changes or even the physiologic response of the body to the lesion; it is essential to note the etiologic factor as well. This, of course, is a general principle of diagnosis, though often neglected, and has been emphasized recently by White in his classification of heart disease. White points out that a comprehensive diagnosis in a patient with circulatory disease should include the following facts: 1, Etiology; 2, structural change; 3, functional condition.

Of all of the different varieties of cardiovascular diseases, lesions of the aorta in particular demand a broad interpretation of all of the facts in the case, because, as I shall endeavor to show, the symptomatology, the course of the disease, its prognosis, and treatment vary considerably, depending upon the underlying etiologic factor.

The main agents that determine valvular heart disease are:

1. The group of rheumatic affections.
2. Syphilis.
3. Arteriosclerosis.
4. Congenital defects.
5. Dilatation of a valvular orifice producing relative insufficiency.
6. Rupture of the valve.

It is very difficult to determine the relative frequency of these various factors. The many statistics that have been published show considerable variation depending largely upon the age distribution and the economic classes of the patients studied. We shall consider this point in relation to aortic disease only.

Of 76 cases of endocarditis that Longcope studied on the autopsy table, 43 gave symptoms and signs during life of aortic insufficiency. In 21 of these the mitral valve as well as the aortic valve was diseased, while the individuals were chiefly children with a history of rheumatic fever. In none of these was syphilitic aortitis present. In the remaining 22 cases, all of which showed involvement of the aortic valves alone, 18, or

81.5 per cent., were associated with syphilitic aortitis. Of 182 cases of aortic insufficiency which Longcope collected from the literature, 74.1 per cent. gave a positive Wassermann reaction.

Broomhead presents the following table:

Aortic Regurgitation	121 cases		
Syphilitic	71 "	= 58.7	per cent.
Rheumatic	50 "	= 41.3	"
Mitral Stenosis	97 "		
Syphilitic	26 "	= 26.8	"
Rheumatic	71 "	= 72.2	"

Patients admitting syphilitic infection, or with a positive or strongly positive Wassermann reaction, are classed as syphilitic.

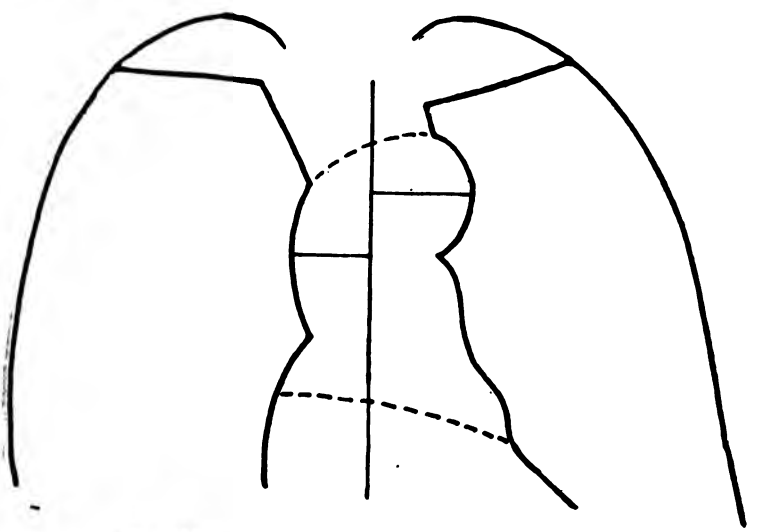

Fig. 113.—Orthodiagram of normal aorta (Vaquez).

Those with a history of one of the rheumatic affections, or with no history of such infection and a negative Wassermann reaction, are classed in the rheumatic group. The number of syphilitics among his mitral cases is much higher than the usual experience in the clinic would warrant. Hubert reported that of the cases of aortic insufficiency studied at Romberg's

clinic, 67 per cent. were luetic, 17 per cent. rheumatic, and 5.5 per cent. arteriosclerotic in origin.

The frequency of syphilis in any group of individuals depends very largely upon the classes of society from which they are recruited. In the male wards of a city hospital positive Wassermann reactions may run as high as 25 per cent. On

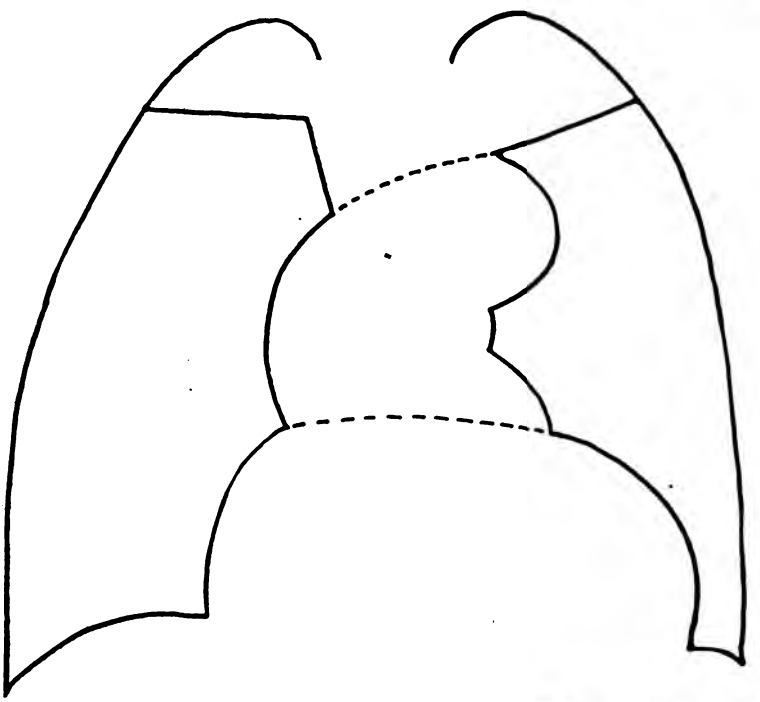

Fig. 114.—Orthodiagram of a case of aortic insufficiency with aortitis (Vaquez).

the other hand, in the routine Wassermann tests which were carried out by the Department of Health in New York City on applicants for license to peddle, 8.4 per cent. were reported positive. In checking a series of 559 hospital patients, the majority of whom were Jews, I found an incidence of 6.2 per cent. of positive reactions among 225 males, and 2.4 per cent. among 334 females. These facts must be borne in mind in

studying the relative frequency of syphilis as a cause of aortic lesions.

An analysis of the cases of heart disease admitted to Montefiore Hospital in the years 1914 to 1921 inclusive is presented in the following table:

TABLE I
(1914–1921)

Ages.	Aortic insufficiency.				Aortic and mitral disease.	Mitral disease.	Total.
	Rheumatic.	Syphilitic.	Arterio-sclerotic.	Total.			
1– 10...	14	..	..	14	11	48	62
11– 20...	51	1	..	52	45	91	143
21– 30...	25	..	..	25	23	48	73
31– 40...	10	3	..	13	10	56	69
41– 50...	6	2	..	8	5	69	77
51– 60...	6	2	3	11	7	45	56
61– 70...	1	4	9	14	6	23	37
71– 80...	...	..	8	8	4	8	16
81– 90...	...	..	..	..	..	2	2
91–100...	..	..	1	1	1	..	1
	113	12	21	146	112	390	536

Patients with valvular disease	536	
Cases of pure aortic insufficiency	6.3	per cent.
Cases of combined aortic and mitral disease	20.9	"
Cases of mitral disease	72.8	"
Patients with aortic insufficiency	146	
Rheumatic	77.4	"
Syphilitic	8.2	"
Arteriosclerotic	14.4	"

While, because of the fact that the majority of patients in this institution are Jews the percentage of syphilitic infection is low, I believe that it may safely be asserted that syphilis of the aorta is less frequent than is generally assumed. Generalizing from this table and from experience in the clinic, one may say that insufficiency of the aortic valve in patients below the age of thirty is usually of rheumatic origin, that between thirty and sixty it is frequently of syphilitic origin, particularly when

it is the only valvular lesion, and that above the age of sixty it is usually due to arteriosclerosis.

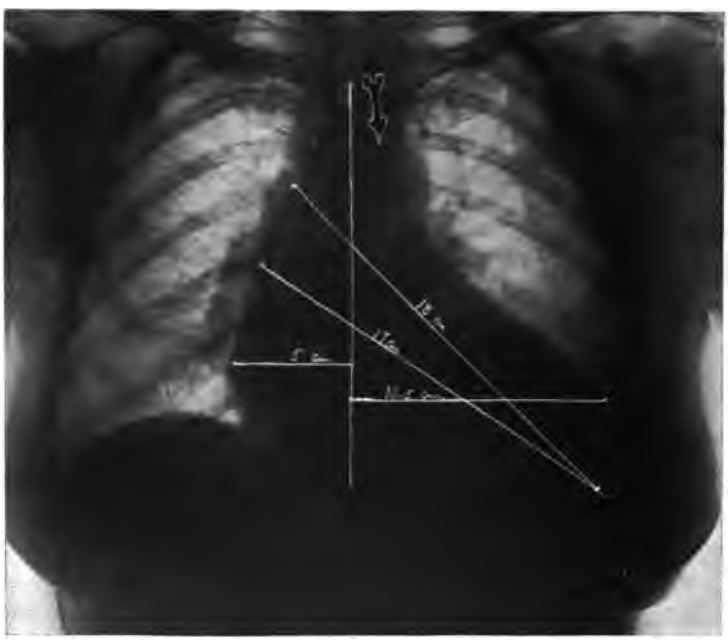

Fig. 115.—Dilated aorta in a case of rheumatic aortic insufficiency.

We shall study the different types of aortic disease, classified according to etiology, illustrating our remarks by the presentation of a few representative cases.

LESIONS OF THE AORTA INDUCED BY THE RHEUMATIC GROUP OF INFECTIONS

It is unnecessary to go into great detail because of the fact that so much has been written on rheumatic heart disease. I shall endeavor to emphasize only a few salient points. In this group are included patients with valvular heart disease which has followed tonsillitis, chorea, and rheumatic fever. With these we must classify for the present cases of valvular heart disease in children or young people who give absolutely no history of

any antecedent infection. It is very difficult to be certain of the etiologic moments in such cases. However, clinically and pathologically they correspond closely with the rheumatic group. It is probable that in them the infection is very insidious, giving rise to few symptoms. The characteristic feature of this group of cases is that the lesions are usually multivalvular. In rheumatic endocarditis it is unusual to find the aortic valve alone involved. In most instances a mitral endocarditis resulting in mitral insufficiency or stenosis is found simultaneously. Myocardial as well as pericardial lesions are common and result in the longer standing cases in irregularity of rhythm. The symptoms of aortic insufficiency in the rheumatic group are usually classical, with a large pounding heart, a high pulse-pressure, and throbbing peripheral arteries. If the mitral lesion is well marked the typical Corrigan pulse is modified and becomes smaller and more sustained. The course of the illness is that of a typical "rheumatic heart" with progression of the disease in exacerbations often due to repeated infections, with progressive myocardial insufficiency. Paroxysmal precordial pain is not a usual feature. The pain is usually that associated with myocardial insufficiency, more or less continuous in character and localized about the apex. The aorta gradually undergoes dilatation, which is rarely extreme.

The existence of a true rheumatic aortitis is doubtful. Albutt describes a number of cases. Osler, on the other hand, states that he has seen only three or four pathologic lesions which could be called rheumatic aortitis. Clinically, the vast majority of cases do not suggest the existence of an inflammatory lesion of the aorta. There are exceptions, however. If we accept Albutt's theory, that angina pectoris is evoked by a lesion that irritates the sensory nerves at the root of the aorta, we should see anginal pain quite frequently in these patients if the rheumatic infection involves the aorta as well as the valves. As a matter of fact, angina pectoris is rare in rheumatic heart disease.

The following case reports illustrate the commoner types of the disease:

Case I. "Silent" Type.—An officer in the army, undergoing

a physical examination prior to promotion, was sent to the base hospital where I was stationed to have his blood-pressure determined. It was 160/40. I thereupon examined his heart, and found definite enlargement, with a distinct diastolic murmur audible along the left border of the sternum. The man had no other signs or symptoms of heart disease whatsoever. There was no throbbing of the vessels, no dyspnea even on severe exertion, and no precordial pain. The patient, a lieutenant in a machine-gun company, was considered one of the best and most active officers in his battalion. For months he had taken his company on daily exhausting drills and had never experienced the slightest distress or symptoms. He gave no antecedent history of infection or of cardiac weakness. The Wassermann reaction was negative. When informed of the fact that he had an organic heart lesion, and that instead of being promoted, he would have to be invalided out of the army, he was overwhelmed with dismay.

This is a typical instance of the so-called "latent" or "silent" type of aortic insufficiency. The patient at some time apparently had had a mild rheumatic infection of the aortic valve, with very slight involvement of the myocardium. His heart hypertrophied, and because of the good musculature and the absence of repeated infections was able to maintain the circulation even under the severest stress. Such patients may go on for many years without experiencing any disabilities, but they are always in danger of further damage to their heart through infection, and of a gradual loss of reserve from overexertion. That is why the man was discharged from the army, although, at the time, he was able to carry on his work better than the average soldier. Such cases are not so very unusual and can be detected only by a routine physical examination with careful attention to the physical signs. Osler mentions a case of a man with such a "silent" lesion who was observed for thirty-five years, during which period he exhibited no symptoms of heart disease.

Case II. Common Type.—The patient is a boy aged fifteen, who, six years previous to his admission to the hospital, had a

severe attack of chorea which lasted for three years and kept him out of school. He has been short of breath since the onset of his chorea. Three years ago he had an attack of rheumatic fever. Two years ago he began to complain of precordial pain in the region of the apex and of pain in the shoulders. At that time a doctor who examined him told him he had heart disease. His chief symptoms since then have been pain and shortness of breath. His tonsils were removed a year and a half ago.

Physical examination showed a well-developed and well-nourished boy, dyspneic on slight exertion, with a dusky flush on his cheeks and cyanosis of the lips. The neck vessels showed a visible pulsation; the lungs were clear. The left border of the heart was 13 cm. from the midline in the sixth interspace and the right border was 4 cm. to the right in the fourth interspace. The apex-beat was forcible and was accompanied by a presystolic and diastolic thrill. At the apex there was heard a rough presystolic and diastolic murmur, as well as a soft systolic murmur. A diastolic murmur of different pitch was heard along the left border of the sternum. The pulmonic second sound was accentuated and reduplicated. The heart rate was rapid and regular. A systolic retraction of the eleventh and twelfth intercostal spaces was observed on the left side in the posterior axillary line. The liver edge was felt 2 cm. below the costal margin. The patient was kept in the hospital for a period of two months, during which time his cardiac reserve gradually increased, and he left the institution with little dyspnea and only occasional precordial pain. The noteworthy features in this case are:

First, the history of chorea and rheumatic fever, followed so closely by shortness of breath.

Second, the involvement of both the mitral and the aortic valves.

Third, the systolic retraction of the chest or Broadbent sign, which indicated the presence of an adherent pericardium.

The rheumatic virus does not attack the valves of the heart alone, but invades the endocardium, the myocardium, and the pericardium, as was pointed out years ago by Corvisart. This

feature differentiates it from the other diseases which affect the aortic valves. Aortic stenosis, associated with aortic insufficiency, although not a feature of this case, is found particularly in rheumatic endocarditis, never with syphilitic insufficiency, and rarely in the arteriosclerotic type of the disease.

Case III. Anginal Type.—The patient is a girl nineteen years of age. When she was nine years old it was noticed that she was weakly and below par. A physical examination then revealed that the patient had an organic heart lesion. Before this she had had measles, scarlet fever, diphtheria, and whooping-cough, but none of the rheumatic group of infections. The following year her tonsils were removed. In spite of this she had occasional attacks of fever, and joint and muscle pains in the following years. She was admitted to the hospital three years ago complaining of pains in the shoulder, dyspnea, and attacks of precordial pain.

Physical examination on admission: A young girl, very dyspneic, with a distinct pallor about the mouth and eyes, flushed cheeks, and throbbing neck vessels. The heart was greatly enlarged, with a heaving apex impulse and a systolic thrill over the aortic area. At the aortic area was heard a rough systolic murmur and a soft diastolic murmur. A pistol-shot sound was audible in the brachial and radial arteries. Ever since her admission to the hospital the patient has had frequent attacks of anginoid pains. She is very neurotic and the slightest emotion or excitement upsets her, causing marked tachycardia and precordial oppression. During the attack the systolic blood-pressure rises to between 250 and 300 mm. Hg. The following is a description of a typical seizure:

The patient suddenly experienced intense pain over the precordium, which radiated to the left side posteriorly and to the right arm. The breathing was rapid and was accompanied by dilatation of the alæ nasi, the face became markedly flushed, with slight circumoral pallor, her head was drawn back and she assumed the position of opisthotonos, which seemed to give temporary relief. The pulsations of the heart and of the per-

ipheral vessels were greatly exaggerated; in fact, the whole body and the extremities were shaken with each heart-beat. The lungs were clear; blood-pressure 300/0. Nitroglycerin was given, which caused a drop in pressure to 194. A few minutes later, however, the attack was renewed, the blood-pressure rose, and the patient complained of a vise-like constriction in her chest.

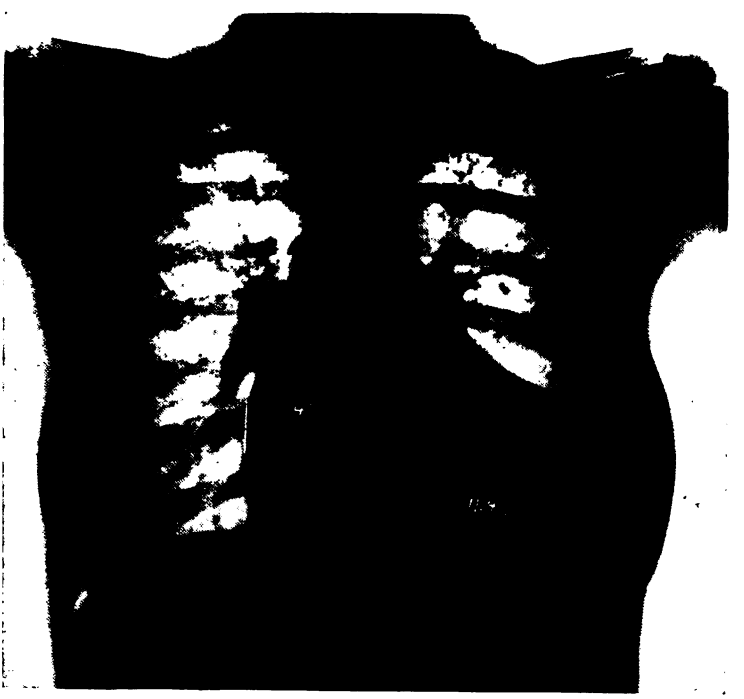

Fig. 116.—Normal aorta in a case of long-standing rheumatic aortic insufficiency. Case III.

These attacks come on at varying intervals and with varying degrees of intensity and have continued to the present. At no time have there been any signs of myocardial insufficiency, such as edema, congestion of the lungs, or enlargement of the liver. Definite zones of hyperesthesia are quite constant over the upper sternum, in the region of the apex, and in the left

paravertebral area from the third to the sixth dorsal spine. During the intervals between the attacks the blood-pressure is approximately 190/0. An *x*-ray examination shows no enlargement of the aorta (Fig. 116). This is especially interesting in view of the long duration of the aortic lesion and in view of the widened area of manubrial dulness. The important features of this case are the anginal seizures, associated with a marked vasomotor disturbance. It is very difficult to determine the nature of these attacks, but in view of the marked pulsation of the aorta, as well as of the other vessels, it is possible that they are associated with involvement of the root of the aorta.

The last case of the rheumatic group which I wish to present, to demonstrate the great difficulty in determining the prognosis, I shall outline only briefly.

Case IV.—The patient was first seen seven years ago, at which time she was about seventeen years of age and had a huge heart with a well-defined aortic insufficiency and mitral stenosis, following several attacks of rheumatic fever. She entered the hospital a number of times in the following years and during the intervals lived a fairly active life at home. During the influenza epidemic of 1918, as well as in the following year, she had a severe attack of bronchopneumonia. She apparently recovered completely from these two infections and soon thereafter married and started housekeeping. About a year and a half ago she visited the clinic, stating that she was three months' pregnant and that she wished to be watched during her pregnancy. Her physical condition was very much the same as on the original examination. She could not be persuaded to have the pregnancy interrupted and justified her determination by giving birth to a healthy baby, without much injury to herself. Such extreme cases, of course, are exceptional, but they do illustrate how great the handicaps are under which the heart will continue to maintain life.

SYPHILITIC AORTITIS

Syphilitic aortitis is one of the most important diseases of the aorta and aortic valves. Although Morgagni had recognized the relationship of syphilis to aortic aneurysm, it was the studies of Döhle in 1888 that placed our knowledge of syphilitic aortitis on a solid foundation. It was not until 1903, however, that the importance of this lesion received general recognition. Since the introduction of the Wassermann reaction attention has been attracted more and more to this manifestation of syphilis. Aortitis is a late manifestation of syphilis, the symptoms first appearing from ten to twenty-five years after the initial infection. More rarely the interval may be as short as three years. Most authors state that this lesion occurs chiefly in persons between the ages of forty-five and sixty years. Longcope, however, in a series of 83 patients, found that 50.7 per cent. were under forty and 80.9 per cent. under fifty, 30.1 per cent. of his cases were under the age of thirty. Schrumpf's cases fell between the ages of thirty-two and fifty. In my own series the patients range between the ages of thirty-one and seventy. A number of cases of aortitis have been described in patients with congenital lues. The disease becomes manifest about the age of twenty. We have observed an aneurysm in a child of thirteen years with congenital syphilis. The disease occurs more frequently in men than in women. It is interesting to note statistics of the incidence of syphilitic aortitis from a slightly different angle. Schrumpf found that of 4280 syphilitic males, over 5 per cent. showed evidence of syphilis of the circulatory system, and that 73.8 per cent. of these had syphilis of the aorta. In Hubert's series of 1380 patients suffering from heart disease, there were 15.5 per cent. with syphilitic aortitis.

The frequent association of tabes and general paresis with aortic disease is noteworthy. In 1879 Berger and Rosenbach pointed out this coincidence, although the common syphilitic origin of these two lesions was at that time unknown. General statistics show that approximately 10 per cent. of tabetics have aortic lesions. The question has recently been carefully studied by Friedman, who found the aorta involved in 14 per cent. of

his own cases. In these cases the cardiovascular infection is discovered usually after the symptoms of cerebrospinal syphilis have been established for several years. In most instances the process is very indolent and chronic in both the nervous system and aorta, so that the symptoms may be few.

The lesion in syphilitic aortitis begins in the media, most often in the ascending arch of the aorta. The transverse and descending portions are the next most frequently involved. The abdominal aorta is rarely attacked. As the inflammatory process descends it involves the semilunar valves and aortic insufficiency may arise. If the orifices of the coronary arteries are implicated, signs of coronary artery disease may appear, and if the wall of the aorta gives way, an aneurysm may develop. In other words, aortic incompetence, coronary artery disease, and aneurysm should be looked upon as complications of a simple syphilitic aortitis. A comprehensive study of the clinical picture, therefore, should concern itself first with simple syphilitic aortitis and then with its complications and the manner in which they affect the clinical picture. It is important, too, to remember that syphilitic myocarditis often accompanies aortitis.

1. **Simple Syphilitic Aortitis.**—This lesion offers many difficulties in diagnosis. The objective signs are usually difficult to determine and unless the symptoms are sufficiently marked to attract attention will be overlooked. The cases are discovered in one of two ways: First, a careful routine study of every known syphilitic patient, including a fluoroscopic and *x*-ray examination, as detailed below, will bring to light a number of cases. The second group of patients are those in whom the symptoms of substernal pain and fear of impending death often resembling those of angina pectoris, dyspnea, palpitation and rapid pulse-rate, draw attention to the heart. These anginal attacks are of great interest and give substantial support to Albutt's theory of the nature of angina pectoris. The pain may be dull and more or less constant and localized behind the sternum, or it may occur in attacks with a sense of constriction in the chest and radiation to the neck and down the arms. Not infrequently a paroxysm of dyspnea is associated with these

attacks. In any patient presenting such symptoms the possibility of a syphilitic infection of the aorta must be considered. An inquiry into the history for a possible luetic infection and a Wassermann test may often clear up the diagnosis. These patients have a rather characteristic grayish pallor, which may draw attention to the nature of their illness. The physical signs, when present, are pulsation felt by the examining finger in the

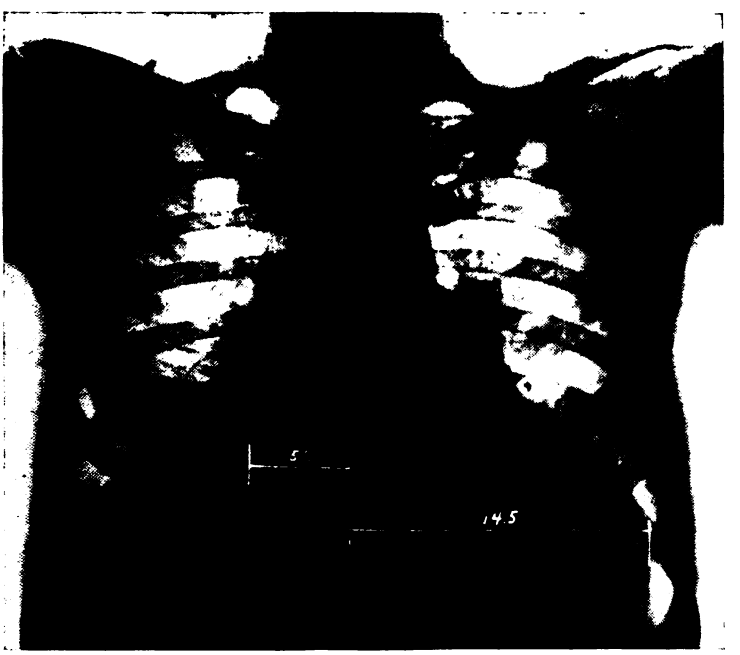

Fig. 117.—Dilated aorta in a case of syphilitic aortic insufficiency with aortitis.

suprasternal notch, pulsation of the right subclavian artery above the clavicle, and dulness in the first and second interspaces to the right of the sternum. The aortic second sound may have a peculiar ringing metabolic quality. A systolic murmur is usually heard at the aortic area. Hoover has recently published a thorough recapitulation of the physical signs of aortitis. By means of the orthodiagraph the diameter of the aorta may be

estimated, its pulsation, contour, and density may be studied. In simple aortitis the transverse diameter of the aorta is increased, the arch is usually elevated, the curves of its contours are accentuated, and its shadow may appear denser than normal. The pulsation may be either diminished or increased. These physical signs and *x*-ray findings, however, occur in all types of aortic dilatation and are not pathognomonic of luetic aortitis.

Arteriosclerosis with dilatation of the aorta, which is so often confused with syphilitic aortitis, is distinguished by the absence of a history of infection or of physical signs of syphilis elsewhere in the body, by a negative Wassermann test, and by the fact that anginal pain is rare in uncomplicated arteriosclerosis of the aorta.

I lay particular stress on the importance of the recognition of uncomplicated aortitis because of the fact that it is these cases which are most hopeful from the point of view of treatment. Once the aortic valves and the coronary arteries become the seat of an organic lesion, or the wall of the aorta has given way to form an aneurysm, treatment will be of little avail, except in so far as it may relieve some of the subjective symptoms.

2. **Aortic Insufficiency.**—The most frequent complication of syphilitic aortitis is aortic insufficiency. Hubert found it in 31.5 per cent. of his patients. In the vast majority of cases it is caused by the extension of the specific inflammation to the semilunar valves. Rarely it is due to a dilatation of the aortic ring, with ensuing relative insufficiency. In these patients there are superadded to the symptoms of simple aortitis the signs and symptoms of aortic insufficiency. Aortic stenosis never develops as a sequence of luetic infection. Whereas, in simple aortitis the heart is rarely enlarged, with insufficiency of the aortic valves left ventricular hypertrophy rapidly becomes manifest. The diastolic murmur is soft and is heard more often along the left border of the sternum than in the second right interspace. It is best heard with the naked ear or with a Bowles type stethoscope. If the bell form is used the murmur may easily be missed. A systolic murmur at the aortic area is invariably present. The presystolic Flint murmur at the apex is

often manifest and may suggest the presence of mitral stenosis. With this there appear the peripheral vascular signs of aortic insufficiency, usually in a more classic form than in the rheumatic group of cases, because of the fact that the mitral valve is not involved, and so does not modify the clinical picture. Throbbing of the carotids is usually manifest, and in more advanced cases the pulsations in the jugular notch and the throbbing of the subclavians above the clavicles is clearly seen and felt. The pistol-shot sound is heard in all of the peripheral vessels. Duroziez's sign can usually be elicited. If the stethoscope is is placed over the external iliac or femoral artery and gradually increasing pressure is exerted, a systolic murmur is immediately audible, which, at a certain degree of pressure, is followed by a diastolic murmur. A systolic flushing of the skin is usually evidenced. It can be readily demonstrated by a brisk rubbing of the skin of the forehead, after which the zone of hypermia will be seen to flush and pale with each heart-beat. Pressure on the finger-nail, of course, will elicit the same phenomenon. In the more extreme cases the head may nod with each heart-beat; in fact, the whole body or even the bed may vibrate synchronously with the heart. The high systolic blood-pressure with the low diastolic pressure and consequent high pulse-pressure are too well known to demand much emphasis. The systolic pressure may vary from 150 to 220 mm. Hg.; the diastolic pressure, from 50 to 0.

Of course, not all of the cases will exhibit these classical physical signs. In fact, the silent type of aortic insufficiency, described in the rheumatic group of cases, occurs in this group as well. This is apparently more frequent in those patients who present a combination of cerebrospinal and aortic syphilis. The anginal symptoms when present are superimposed on the signs and symptoms of valvular disease.

Another group of symptoms found in these patients are those of progressive myocardial insufficiency. These do not require particular description because they correspond to those found in all cases of cardiac failure. The majority of patients with syphilitic aortic insufficiency die of cardiac failure; some

die during an attack of angina pectoris. Still another interesting termination of this disease is an infective endocarditis. It is common knowledge that the subacute infective endocarditis caused by the Streptococcus viridans is engrafted on an old valvular lesion, which is generally of rheumatic origin. Syphilitic disease of the aortic valves occasionally is the precursor of this malignant infection.

3. **Coronary Artery Disease.**—The symptoms of coronary artery disease are usually impossible to differentiate from the symptoms of angina pectoris. Pathologically the lesions are due to an extension of the inflammatory lesion of the aorta in the sinuses of Valsalva, where the mouths of the coronary arteries are encroached upon. It is very difficult to distinguish this group of cases from the others, for all of the cardinal symptoms of angina pectoris may be present even when the coronary arteries are perfectly healthy.

4. **Aneurysm of the aorta** is the other complication of syphilitic aortitis which must be mentioned; 16 per cent. of Hubert's patients with aortic disease presented this lesion. I shall not discuss the specific physical signs and symptomatology of aneurysm, but mention it to emphasize its relationship with the other forms of aortic disease. Probably 85 per cent. of all aneurysms are due to syphilis. The age incidence is the same as that of the other types of syphilitic aortitis. It is important to remember that an aortic aneurysm is frequently unassociated with lesions of the aortic valves and unaccompanied by cardiac hypertrophy. It may be associated with symptoms of angina pectoris. I shall not discuss in this clinic the signs and symptoms brought on by the pressure of the aneurysm on adjacent organs.

Let us summarize briefly the important facts concerning syphilis of the aorta that have been detailed above. Syphilitic aortitis may occur with or without involvement of the aortic valves or coronary arteries and with or without the presence of an aneurysm. It is a frequent form of visceral syphilis and is often associated with the late forms of cerebrospinal syphilis. The symptoms of aortic involvement occur about twenty years after the initial infection. Once they have become established,

however, the downward course of the patient is rapid. Death usually occurs within from one-half year to two years after the symptoms have become manifest. Of course, the lesion in the aorta probably considerably antedates the symptoms. The causes of death are detailed in the following table taken from Hubert:

Cause of death.	Intercurrent disease.	Myocardial insufficiency.	Angina pectoris.	Rupture.
Aortitis	12	5	3	
Aortic insufficiency	2	5	1	
Aneurysm	5	5	4	6

Treatment.—The treatment of syphilitic aortitis resolves itself, first, into treatment of the syphilitic infection; second, of the accompanying symptoms. It would seem that the principles underlying the treatment of lues would remain the same irrespective of what part of the body happens to be invaded by the syphilitic virus. However, when salvarsan was first introduced, a warning was issued not to employ it in cases of cardiovascular syphilis. In the course of time, however, many began to use it in these patients with good results, so that today few hesitate in the employment of salvarsan or one of its derivatives in luetic disease of the heart and aorta. Quite recently, however, Wile has again called attention to the dangers of a too intensive therapy. He cites cases in which intensive treatment with salvarsan was followed by acute myocardial insufficiency or by the rupture of an aneurysm. Others before him have pointed out this danger. It is safer to begin treatment with a course of mercury and potassium iodid lasting several weeks, and to follow this with the arsenical. Neosalvarsan is the most convenient form of the drug to use. It is well to start with a dose of 0.2 gram, and if this is borne well to increase the dosage gradually to 0.9 gram. Six doses of salvarsan may be given, and then after a rest of a month the whole treatment should be repeated.

The results of treatment will depend on the nature of the individual case. In uncomplicated aortitis we may hope to arrest the process and to prevent the development of the graver

lesions. In aortic insufficiency and aneurysm less improvement can be expected. In some instances we may be able to arrest the progress of the lesion. The most striking result of the treatment is in the improvement of the general condition, in a gain in color, weight, and strength. Very often we are able to relieve the attacks of precordial pain and to diminish the dyspnea. In all cases prolonged treatment is necessary.

There is a question whether all patients should be submitted to intensive treatment. Certain indolent lesions of the aorta, especially those associated with tabes, seem to give the patient very little trouble. We may well hesitate in these cases for fear of stirring to activity the dormant infection.

The treatment of these patients, aside from the treatment of their syphilis, is the same as that of others with heart disease. With myocardial insufficiency the restriction of fluids, bed rest, and the administration of digitalis are the main stays. Aortic insufficiency is not a contraindication to the use of digitalis. Instead of going into greater detail about the common-sense therapy of these patients, I shall present to you a few interesting cases that will illustrate a few of the points that we have been discussing:

Case V.—The first patient is a man seventy-two years of age, who entered the hospital complaining of inability to stand or walk, and of incontinence of urine and feces. He had a chancre thirty-five years ago, which was inadequately treated. He was always in good health until two and one-half years before his admission, when he began having difficulty in walking, which became progressively worse. Nine months ago the loss of sphincter control became manifest.

Physical examination revealed fixed irregular pupils, absent knee-jerks, and other signs indicating a cerebrospinal syphilis. The heart was not enlarged. The aortic second sound was accentuated and metallic in quality, and was accompanied by a systolic murmur. The blood-pressure was 102/62. The Wassermann reaction was positive. After a year in the hospital, during which he presented no symptoms referable to the

heart or aorta, the patient died of an intercurrent bronchopneumonia. Autopsy revealed the aorta diffusely dilated, especially the arch, and covered throughout with large atheromatous and atherosclerotic plaques, with moderate puckering and parallel streaking of the intima. The heart exhibited no abnormality. This case illustrates the latent or silent type of simple syphilitic aortitis, giving rise to no symptoms. It also shows the long interval between the initial infection and the development of the aortic lesion, as well as the association of aortitis with cerebrospinal syphilis.

Case VI.—A patient forty-one years of age entered the hospital complaining of attacks of pain in the precordium which extended to the neck and left arm. His past history was absolutely negative except for an appendectomy in 1920. There was no history of venereal infection. He married at the age of thirty. His wife had 3 children, all of whom are living and well, and had no miscarriages. Seven months before his first admission, while walking in the street, he suddenly experienced great difficulty in breathing and had to stop to catch his breath. At the same time he felt a numbness of the fingers of the left hand. This attack lasted fifteen minutes, after which he took the subway to go to work. When he got out of the train the attack was repeated, but he now experienced pain in his left hand, which then extended up to the neck and to the region of the heart. Ever since this time he has had many similar attacks, usually two to three a day.

Physical examination revealed a slightly built man, fairly well nourished. The heart exhibited the classical signs of aortic insufficiency with considerable enlargement, a diastolic murmur heard with the greatest intensity along the left border of the sternum, marked pulsation of the peripheral vessels, blood-pressure 145/50. There were no clear-cut signs of involvement of the central nervous system, but the pupils were a bit sluggish and the reflexes were exaggerated. The Wassermann reaction of both blood and spinal fluid was positive. The area of aortic dulness was increased. The *x*-ray examination showed

the heart enlarged both to right and left (duck shaped) and the knob of the aorta prominent.

During his stay in the hospital the patient had frequent attacks somewhat like those described above. There undoubtedly was a large functional element in them, but nevertheless there was a definite anginal substratum. Neosalvarsan was administered beginning with a dose of 0.2 gram and continued at weekly intervals until a final dosage of 0.9 gram was administered. Eight doses were given, and then, after a month's rest, another series of six doses were given combined with a course of mercury salicylate. The attacks of pain disappeared within a few weeks after the treatment was commenced and did not return. The patient was discharged from the institution after six months. Three months later he was readmitted to the hospital complaining of the same seizures, which had recurred soon after his return home. There was no change in the physical signs.

This patient again shows the association of aortic and cerebrospinal syphilis, but, in addition, presents definite attacks of angina pectoris.

Case VII.—The next patient whom I wish to present was seen through the courtesy of Dr. Walter M. Kraus. He was a man fifty-one years of age, who had a chancre thirty years ago. For many years he had been immoderate in the use of food, alcohol, and tobacco. Six weeks before his admission to the hospital he developed a right hemiplegia, since which time he has been confined to bed.

Physical examination revealed tabes dorsalis associated with a right hemiplegia. An interesting feature was the fact that following the hemiplegia the right knee and Achilles' jerks, which had been absent, became quite active. A Babinski was present. The heart showed tremendous hypertrophy with a widening of the aortic dulness, marked pulsation in the jugular notch; a loud diastolic murmur heard all over the precordium, and a systolic murmur at the aortic area. The blood-pressure was 165/40; respirations were rapid and the lungs showed many

râles at both bases. The temperature ranged from 101° to 103° F. There were no chills. Because of the fever and the lung signs a diagnosis of bronchopneumonia was first made. However, within a few days, large groups of petechiæ appeared scattered all over the trunk and extremities, and two were noted in the right lower conjunctiva. The conjunctival petechiæ, as well as many of the cutaneous ones, had well-marked white centers and were, therefore, pathognomonic of Streptococcus viridans infective endocarditis. Several blood-cultures revealed many non-hemolytic streptococci. A blood-count showed a polynucleosis. The Wassermann reaction of the blood and spinal fluid was negative. The urine, in addition to albumin and casts, showed numerous red blood-cells. In view of the presence of the bacterial endocarditis the pulmonary signs were interpreted as infarcts. The patient lived for five weeks and showed no new or embolic phenomena, with the exception of repeated new groups of petechiæ in enormous numbers.

The pathologic examination confirmed the clinical diagnosis of syphilitic aortitis with a superimposed vegetative endocarditis, which involved not alone the aortic valve, but the tricuspid and mitral valves as well. The lungs presented multiple infarcts.

This patient illustrates the sequence of an initial infection thirty years ago followed by tabes dorsalis and later by invasion of the aorta with subsequent aortic insufficiency. The cardiovascular involvement caused few symptoms. The bacterial endocarditis was engrafted on the old luetic valve lesion and had existed probably several months before the death of the patient. We arrive at this opinion because of the hemiplegia eleven weeks before the patient's death, which was probably caused by an embolus from one of the vegetations of the aortic valves. Of course, it is a question whether the cerebral injury was due to a syphilitic cerebral vascular lesion or to an embolus.

ARTERIOSCLEROSIS OF THE AORTA

Arteriosclerosis of the aorta, just as arteriosclerosis elsewhere in the body, occurs most frequently in individuals above the age of sixty. It involves the arch and the thoracic portion of the aorta, just as does luetic aortitis, but it frequently extends to the abdominal aorta as well. Of course, early atherosclerotic lesions are common even in young people. I have reference here to changes sufficiently advanced to give symptoms or physical signs.

It may be well to briefly discuss a few common assumptions about arteriosclerosis that too often go unquestioned. In the minds of many arteriosclerosis is closely associated with high blood-pressure. This relationship is quite inconstant, and it is not at all unusual to find advanced sclerotic changes in the aorta or, for that matter, in other vessels with a normal blood-pressure. As a matter of fact, it is the decrescent type of arteriosclerosis of Allbutt that causes the greatest deformity of the vessels. With hypertension there may be a diffuse dilatation of the aorta without much change in the intima. The patients who show marked calcification and deformity of the intima, however, often have a normal arterial tension. Second, it is customary to feel the radial and temporal arteries, or possibly a few more peripheral vessels, and to infer from their condition the degree of change in the aorta. It has been shown by careful pathologic studies that such an association is not at all constant. A comparison, for instance, of the degree of sclerosis of the aorta, the peripheral, coronary, and basilar vessels, showed that one group might be diseased, while the others were normal, and that no predictions could be made from the condition of one set of vessels as to what might be found in the others.

With the exception of the fact that in uncomplicated arteriosclerosis of the aorta angina pectoris is infrequent, the clinical picture resembles a good deal that of syphilitic aortitis. The differentiation, however, is an important one to make because the course of the disease is slower and the prognosis for the duration of life much more favorable.

These patients, too, may be classified into those in whom

there is a simple involvement of the aorta, those in whom the process has involved the aortic valves as well, and those in whom the coronary arteries are encroached upon. The symptoms and physical signs of the different groups correspond largely to those of the syphilitic patients.

Advanced sclerosis of the aorta results in dilatation and lengthening of the vessel. This is evidenced by increased dulness in the first two interspaces to the right of the sternum, by pulsation in the jugular notch, and by pulsation of the subclavian artery above the clavicle. The radioscopic signs resemble those previously described. The heart is not enlarged, the second aortic sound is accentuated, and there is usually a systolic murmur audible at the aortic area.

When the semilunar valves are included in the atherosclerotic process the symptoms and signs of aortic insufficiency are superadded. Aortic stenosis may develop in contradistinction to syphilitic disease. When the orifices of the coronary arteries are sclerosed attacks of angina pectoris may occur. When this happens the prognosis becomes grave. Either the patient dies from acute coronary closure, or else the impaired nutrition of the heart muscle and the frequent closure of smaller branches of the vessels cause myocardial degeneration, with progressive myocardial insufficiency. The myocardial lesions may cause cardiac irregularity. Auricular fibrillation is the most frequent arhythmia encountered.

Arteriosclerotic disease of the aorta is of slow development and often causes few symptoms. Even when aortic insufficiency develops, they may be insignificant. Coronary artery disease is the most frequent cause of distress in these patients. But even in these cases we have learned that if the occlusion of the vessels is a very gradual one, large areas of heart muscle may be destroyed without causing the patient very great inconvenience. The anastomoses of the coronary arteries, in particular the fat vessels in the epicardium, are able to carry on a circulation sufficient to the restricted needs of the individual.

Death comes from myocardial insufficiency or from intercurrent disease.

In patients with hypertension, dilatation of the aorta is seen, which is often unassociated with arteriosclerosis. The signs of such dilatation do not differ from those already described.

Case VIII.—The next patient to be presented, seventy-five years of age, was admitted to the hospital two years ago for a right hemiplegia, which had come on a month previously. His history previous to this time was not significant.

The physical examination shows an elderly man, well nourished, somewhat pale, who walks about with a typical hemiplegic gait. Aside from the hemiplegia he shows a moderate emphysema; the heart is not enlarged. The aortic second sound is accentuated and is followed by a short diastolic murmur. There is also a systolic murmur at the aortic area. There is no widening of the area of aortic dulness. Blood-pressure 178/62. The radial arteries are not much thickened, but the brachials are tortuous and nodular. The temporal arteries are slightly tortuous. The urine shows a faint trace of albumin and occasional casts. The phenosulphonephthalein excretion is 29 per cent. in two hours. The blood nitrogen is normal. The blood Wassermann is negative. During the two years of his stay in the hospital there has been little change in the patient's condition. He has few complaints and is up and about most of the time. He occasionally shows edema of the legs. This is a typical case of arteriosclerotic involvement of the aortic valves, which gives rise to few symptoms. Because of his hemiplegia, of course, the patient is not very active and the heart is able to meet the demands placed upon it. The hemiplegia is due apparently to a cerebral hemorrhage or thrombosis. The aortic disease has little effect upon his general condition and will not be an active factor in causing his death.

For the sake of completeness we may mention two other types of aortic disease. The first is aortic insufficiency due to rupture of a valve leaflet. This is uncommon and usually occurs in a previously diseased valve. The following case gives a typical picture of this condition. An undertaker, previously healthy, one day while carrying a heavy coffin up a flight of

stairs experienced a sudden sharp pain in his chest and fainted. For some weeks after this he had palpitation, dyspnea, and a rapid pulse. The symptoms gradually quieted down, but he has never recovered his complete strength and becomes short of breath on moderate exertion. On physical examination he presents a typical aoritc insufficiency with a very large heart and the other usual signs.

Finally, it is well to remember that occasionally disease of the aortic valves with either stenosis or insufficiency may be due to a congenital malformation of the cusps. This should always be kept in mind in aortic valvular disease in children, and even in adults, if the heart disease can be traced to early life. An infective endocarditis engrafted upon the congenital defect is the most frequent cause of death in these patients.

In closing I wish again to emphasize the importance of determining the etiology of every aortic lesion, and of accuracy in the terminology used to describe the lesion. We should speak of rheumatic, syphilitic, or arteriosclerotic aortic valvular disease, as the case may be. Dilatation of the aorta may occur in a variety of conditions and is not synonymous with aortitis. The latter term should be reserved for the syphilitic type of the disease and for the rare acute inflammations of the aorta. Arteriosclerosis of the aorta with dilatation conveys a definite idea of the pathologic process.

Accuracy in terminology leads to clearer concepts of disease and to better and more intelligent care of the patient.

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CLINIC OF DR. RUSSELL L. CECIL

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THE MANAGEMENT OF EARLY CASES OF CHRONIC INFECTIOUS ARTHRITIS

I WISH to present to you today several cases of chronic infectious arthritis or, more properly speaking, cases that have been chronic arthritis, but which are now normal or practically normal healthy individuals. In this presentation I have purposely omitted gonococcus infections of the joint, for while this type of arthritis is often obstinate and may even end in ankylosis, it rarely runs the course of a true deforming arthritis.

The 4 cases which I will present to you today have this much in common, that they are all ambulant cases and were, therefore, seen fairly early in the disease. The advantage of treating any infectious disease in the incipient stage is well recognized by all practitioners, and this advantage applies with particular force to chronic arthritis. It is obvious that an inflamed joint will be more amenable to therapeutic measures before dense fibrous tissue has invested the part, with obliteration of the articular surface and formation of a thick capsule about the joint.

I wish today to emphasize the infectious nature of chronic arthritis. For this reason I have selected 4 cases which illustrate various types of focal infection:

Case I.—Chronic Arthritis Associated with Chronic Tonsillitis.—Young woman, twenty-eight years of age, stenographer. Admitted to clinic September 25, 1913, complaining of pain in joints.

Past History.—No history of chorea or rheumatic fever. No heart trouble. Has always enjoyed good health. Rarely catches cold, but seven years ago she had an attack of acute tonsillitis. At that time she was sick two weeks with fever and very sore throat. No pains in joints at that time.

Present Illness.—One year ago she had a second attack of acute tonsillitis; about two months later she began to have pain in her joints, first noticed in the right elbow, which was red, swollen, and painful on motion. A little later the left elbow became involved. Since then the following joints have been implicated: right wrist, right elbow, left knee, and both heels. A few days ago she noticed pain in the back of her neck.

Present Examination.—Patient is a well-nourished, well-developed young woman. Teeth are in excellent condition. Tonsils are small, red, and very hard. On pressure pus exudes from the crypts. The right elbow is swollen and tender, there is slight inhibition of motion. The right wrist is also swollen and slightly reddened. There is definite tenderness over both heels.

x-Ray plates of the various joints showed no injury to the articular surface. Cultures from the tonsillar crypts yielded an almost pure growth of Streptococcus viridans.

In view of the history and physical finds tonsillectomy was advised, and the tonsils were removed in December, 1913.

For one month following the operation patient felt a great deal better. The stiffness and pain in the joints disappeared almost entirely. Then gradually the symptoms returned. When she returned to the clinic April 24, 1914 there was very little evidence of arthritis except pain and stiffness on motion of several of the larger joints. When her throat was examined, however, it was clear that the right tonsil had not been completely removed. On that side there was a small remnant of tonsillar tissue, knarled and red, and just above the right tonsil there was a small ulcer which contained pus. Culture from this pus-pocket showed many colonies of Streptococcus viridans. On this occasion it was decided to make an autogenous vaccine for the patient. Vaccine was prepared from the Streptococcus viridans, and on May 8, 1914 she received a dose of 50,000,000

subcutaneously. Patient had considerable focal and constitutional reaction from this inoculation, but felt better the next day. On May 13, 1914 the remnant of right tonsil was removed and found to contain pus. The inoculations of vaccine were continued and patient frequently showed focal reactions in the left knee after the injections. Some of these focal reactions were quite severe, but they were temporary, and in twenty-four hours the patient felt a good deal better.

May 22, 1914: Patient shows considerable improvement. She says she hasn't felt so well for weeks. Much less stiffness in knee and ankle.

June 27, 1914: Still receiving vaccine and continues to improve.

July 9, 1914: Patient received 1,000,000,000 streptococci subcutaneously. She is now practically well, but still gives some reaction to vaccine.

July 25, 1914: The patient was discharged and was not seen again until February 15, 1915, nearly seven months later. At this time she complained of pain in right elbow and left knee, one month in duration. One week ago the right knee began to pain her.

Examination of throat shows a small pocketful of cheesy material just above the site of the left tonsil. Culture shows Streptococcus viridans in large numbers. The pocket was split open to allow better drainage and a new vaccine was prepared.

February 22, 1915 patient received 100,000,000 new streptococcus vaccine and inoculations were continued every four or five days in increasing doses. Patient made rapid improvement, and was discharged again on March 20, 1915 entirely free from symptoms.

The fourth and last attack of arthritis which occurred in this patient developed November 11, 1916, one year and seven months after the previous attack. On this occasion the symptoms were mild. She came in complaining of pain in the right fifth metacarpophalangeal joint and slight twinges in the left elbow. The small pocket above the site of the left tonsil which had been opened up after the last attack was still present in spite of

the previous operation, and contained a small amount of pus. Culture showed Streptococcus viridans. A new vaccine was prepared and inoculations were given subcutaneously every four or five days. Dobell's solution was prescribed for gargling twice a day. One month after the initiation of treatment patient was feeling better, but there was still some pain. At this time she was put on a low carbohydrate diet. Patient was referred to laryngologist, who felt that the small pocket in the throat was entirely innocuous.

March 30, 1917: Argyrol prescribed for throat, baking and massage for finger. Patient made a gradual but complete recovery, and has had no recurrence since, though several years have passed since the last attack.

The interesting feature about this case is the close relationship which existed between tonsillitis and arthritis. This case also teaches the importance of complete and thorough enucleation of the tonsil. A small fragment of the diseased right tonsil was sufficient to bring on a second really severe attack of arthritis. It will be observed that practically no medicines were used in the treatment of this case. Autogenous vaccines apparently had a definite effect. I am not an advocate of vaccines for every case of arthritis, but I do think that in the obstinate types the patient should have the benefit of vaccine treatment, for there are certain cases that appear to respond favorably to vaccine therapy, particularly if the inoculations are followed by focal reactions in the joints. I suspect, however, that in this case the persistent treatment of the tonsils and the pockets which remained after the removal of the tonsils had more to do with the patient's recovery than did the injections of vaccine. The massage and bakings were also beneficent factors.

Case II.—Chronic Arthritis Associated with Apical Alveolar Abscess.—J. G. B., aged thirty-eight, clergyman. First seen October 14, 1920, complaining of pain in left knee-joint. Family history negative.

Past History.—No previous attacks of rheumatism. Twelve years ago he had an attcak of tonsillitis and has had several

attacks since, the last one occurring about one year ago. He is not susceptible to colds, but when he does contract a cold his frontal sinuses become involved. Influenza in 1918. Venereal disease denied. Bowels regular.

Present Illness.—About sixteen months ago patient gradually developed pain and stiffness in the right hip-joint. Thirteen months ago he had an attack of tonsillitis followed by immediate relief from pain in the hip. Three months ago his left knee became swollen, painful, and stiff. At present the knee is still very painful and there are also twinges of pain in both wrists.

Physical Examination.—Well-developed young man, good color, many teeth filled and several crowns. No pyorrhea. Throat appears normal; tonsils almost invisible. No pus in crypts. Lungs, heart, and abdomen negative. Left knee-joint is not noticeably swollen, but there is slight tenderness on pressure and flexion is considerably limited. Patient walks with a decided limp. *x*-Ray of left knee practically negative. Laryngologist reports that tonsils do not show enough change to justify tonsillectomy unless all other sources of infection can be eliminated. *x*-Rays of teeth show several large root abscesses.

November 16, 1921: Patient referred to dentist, who extracted 5 teeth. Culture from the root abscesses showed pure growth of Streptococcus viridans. Following the extraction of the teeth patient began to make immediate improvement, and in a short time the stiffness and pain had entirely disappeared from the knee-joint and patient was able to resume his regular vocation. There has been no return of symptoms since that time.

Remarks.—This case shows the close relationship which often exists between apical abscesses and chronic arthritis. The history of this case was a little confusing, as the patient had had several attacks of tonsillitis. Strangely enough, the last attack of tonsillitis appeared to act as a specific therapeutic agent against an incipient arthritis of the right hip. This patient received neither medicine nor vaccine, but made a rapid recovery as soon as the apical abscesses were drained.

Case III. Chronic Arthritis Associated with Paronychial Infections.—C. B., salesman, aged thirty-five. Admitted to Cornell Clinic September 22, 1922, complaining of pain in joints.

Family history negative.

Past History.—Pneumonia in boyhood. No other serious illnesses. Two years ago he had his tonsils removed and several teeth extracted. At the same time the nasal septum was straightened. Venereal infection denied. Appetite good. Bowels regular.

Present Illness.—Arthritis began ten years ago with pain and stiffness in back and neck. Has been getting progressively worse. For a considerable period of time the disease was limited to the spine. During the last two years, however, the feet and knees and to a less extent the hands have become involved. Otherwise patient's health is good.

On admission patient complains of pain, swelling, and stiffness in ankles and knees. His back is stiff, but causes him little or no pain.

Physical examination shows well-developed, well-nourished adult. The patient walks with decided step and with both feet everted. Pupils equal and react to light and accommodation. Teeth and gums in good condition. Throat appears normal, no tonsils visible. Lungs and heart negative, abdomen negative. The spine is obviously the seat of an old ankylosing spondylitis. There is a marked rigidity in the lumbar region and rigidity with kyphosis in the upper dorsal and cervical region. There is swelling and tenderness in both feet and ankles, with considerable rigidity. The knees are both swollen and painful on motion, but there is no evidence of ankylosis. There is some stiffness and pain in the right shoulder.

An interesting lesion was found on both great toes. They showed marked ingrowing of the toe-nail, and around the nail there was considerable swelling, redness, and induration of the tissue. On pressure a considerable amount of pus oozed out around the nails. Patient was admitted to Bellevue Hospital, Ward A-1, for further study. Two teeth were extracted and a

prostatic massage was performed in order to obtain cultures from the prostatic secretion. These cultures were negative. Cultures from the pus about the great toe-nails showed in both instances an almost pure growth of Streptococcus hemolyticus. Wassermann test negative. Blood-sugar 150 mg. per 100 c.c.; uric acid 4.2 mg. On account of the bacteriologic findings in the toes patient was transferred to the surgical side and both nails were removed under local anesthesia. The wounds healed nicely and following the operation patient began to show almost immediate improvement. There was little or no change in the spine, which was obviously an old process, but the swelling in the ankles and knees began to disappear and the patient walked with a great deal more comfort.

An autogenous vaccine was prepared from the Streptococcus hemolyticus which had been isolated from the paronychia.

October 8, 1922: Patient received 10,000,000 streptococcus intravenously. This injection was followed by a mild chill and a slight rise of temperature.

October 12, 1922 patient feels so much better that he insists on leaving hospital. Promises to return for further injections of vaccine.

This patient has not been seen since his discharge. His improvement was so marked, however, that there could be little doubt about the relationship between the paronychia and the arthritis. In this case it was interesting to note that the joints involved were the feet, ankles, and knees—just what one might expect if the infection was due to the paronychia and was extending upward through the lymphatics. This case illustrates the rather rare group of arthritides in which the focus of infection is found outside the oral cavity.

Case IV.—Chronic Arthritis Associated with Chronic Colitis.—L. D., housewife, aged fifty-four. First seen June 1, 1921, complaining of pain in joints.

Family history negative.

Past History.—Always enjoyed good health until the birth of her child twenty-three years ago, when she was left with a

badly torn perineum. An immediate perineorrhaphy was done, but the stitches tore out. Four years later a second operation was performed, but a sinus remained and recovery was greatly prolonged. Since then the patient has had difficulty in emptying bowels and has had to resort to frequent enemas. Six years ago a hysterectomy for fibroids was performed. Patient suffers a good deal from weakness and indigestion. In 1914 she had a severe sore throat which was epidemic at the time. This epidemic was traced to a Streptococcus hemolyticus in the local milk supply. Since that time patient has suffered with pain and stiffness in neck and shoulders, which at times has been so severe that she has been unable to walk. Patient is constipated and has considerable gas. For several years she has been troubled with periodic attacks of mucous colitis.

Present Illness.—During the summer of 1920, one year before admission, patient suffered a great deal with severe indigestion and stomatitis and became extremely depressed. On a low carbohydrate diet she improved rapidly and did well until February, 1921, when she began to have severe pain in the neck, shoulders, and left arm. Rheumatism was so severe that she was confined to bed.

April 1, 1922, three months ago, patient suddenly developed signs of acute intestinal obstruction. An emergency laparotomy was performed and a kink was discovered in the lower ileum. Gall-bladder, stomach, and pylorus were apparently normal. Following the operation patient was extremely ill. She developed a double parotitis which was very painful and which required considerable morphin. Temperature 101° to 102° F. Cultures showed Staphylococcus aureus. Immediately following the operation the pain in her joints was quiescent, but as her general condition has improved the arthritis has increased in severity, and at the present time the hands and knees are swollen, tender, and painful. There is also a great deal of pain in the right arm, but this appears to be of muscular origin.

Physical Examination.—A fairly well-nourished woman, middle aged, chronically ill. Temperature normal in the morning, with afternoon elevation to 100° or 101° F. Teeth in ex-

cellent condition. Tonsils appear normal. Lungs and heart normal. Abdomen negative except for operation scars. Extremities: Both arms show considerable muscular atrophy and the muscles are quite tender on pressure. Motion in the right arm is painful, especially at the elbow, but this appears to be due to muscular involvement rather than in the joint itself. The fingers all show fusiform enlargement of the first phalangeal joints, and the metacarpophalangeal joints are also involved. The left arm shows changes similar to the right, but not so severe. The fingers of the left hand are swollen and tender like those of the right. The backs of the hands are puffy. Both wrists are swollen and tender, the right worse than the left. Motion is extremely painful. The knees and ankles are swollen, tender, and painful on motion, and the feet are tender on pressure, particularly in the soles. There is tenderness over the cervical spine and pain on flexing and rotating the neck. *x*-Ray photographs of the spine and of the knee-joints show early bony changes. The lesions in the fingers appear to be entirely periarticular. The urine is negative.

Cultures from the tonsils showed the normal mouth flora. Cultures from the stool yielded the colon bacillus and the usual inhabitants of the large bowel. In addition, however, a few colonies of Streptococcus hemolyticus were found on the plates.

Discussion.—Here was a case in which several factors had to be considered. The tonsils and teeth could be eliminated with a fair degree of certainty, although the patient did give a history of one severe attack of tonsillitis. The genito-urinary tract had presented no symptoms since hysterectomy ten years before the arthritis developed.

Perhaps the most significant point in the patient's history was the existence of a chronic colitis from which she had suffered for a number of years. The patient was a very intelligent woman and stated that with each exacerbation of her colitis there was a subsequent exacerbation of the arthritis. This history, taken in conjunction with the finding of hemolytic streptococci in her stools, pointed rather strongly toward the large intestine as the primary focus of infection. An autogenous vaccine was pre-

pared from the Streptococcus hemolyticus which had been isolated from her stools.

On June 6, 1921 subcutaneous inoculations were started, the patient receiving 100,000,000 streptococci in the first injection. Injections were repeated every four or five days with gradually increasing dosage. With every injection of vaccine there was a sharp exacerbation of pain in the joints.

On June 13, 1921 the patient was started on Bacillus bulgaricus injections per rectum twice a week.

On June 21, 1921 patient received 0.5 gm. of foreign protein (secondary milk proteose) intravenously. There was no chill, but the temperature arose shortly after the injection to 100.5° F. and patient suffered general malaise for two hours, with gradual return of temperature to normal.

July 1, 1921: Patient showed no improvement as the result of vaccine treatment or foreign protein injection. Vaccine treatment continued.

July 15, 1921: Patient began to receive high colon irrigations containing ichthyol every day +; also received 1 gm. secondary proteose intravenously. Following the injection there was a sharp chill, with rise of temperature to 103° F. Patient felt very uncomfortable during the reaction.

July 17, 1921: Patient shows distinct improvement following foreign protein injection. There is less pain in both arms and patient is up in wheel chair.

August 1, 1921: Patient continues to improve. Baking and massage started. Arms and legs exposed to sunlight every day.

August 15, 1921: Still improving. Today received 1 gm. of secondary proteose intravenously, followed by sharp reaction similar to previous reaction.

From this point on patient made a slow but gradual recovery. No more foreign protein injections were given, but the baking and massage were continued regularly every day and the colon irrigations were also continued.

In this case autogenous streptococcus vaccine appeared to confer no benefit. On the other hand, the intravenous injections of foreign protein seemed to mark a turning-point in the patient's

illness. Following the second injection she began to improve and continued to improve thereafter. Baking and massage were undoubtedly instrumental factors in her recovery, and certainly the ichthyol irrigations, by keeping the large bowel in good condition, helped to overcome the infection. At one time we considered this patient incurable, but she surprised those of us who had studied her by making a complete recovery.

Every case of arthritis is a problem in itself. No two cases are alike, and each one presents itself as a small problem in medical research. In any attempt to locate the cause of the infection an accurate history is of the greatest importance. Personally, I attach considerably more importance to the history than to the physical examination. In taking the history one should make particular inquiry concerning attacks of tonsillitis, alveolar abscesses, sore throat, colds, etc. In a certain number of cases the patient will give a history of arthritis setting in after a severe cold. In these cases there may be no evidence of infection in the tonsils or in the sinuses at the time the patient is seen. It is reasonable to suppose that in such instances infection gets into the joints at the time of the cold and no trace remains of the primary infection. A careful genito-urinary history should also be obtained from patients of both sexes, for next to the oral cavity the genito-urinary tract is the most important site for focal infections. Next in importance I should place the gastro-intestinal tract, and a history of colitis, gallstones, or appendicitis should be carefully recorded.

The physical examination is important, especially in respect to the oral cavity and the extremities. In early cases of arthritis the patient usually looks healthy. As a rule, the lungs, heart, and abdomen are normal. The tonsils and teeth should be examined with particular care, and in most cases I prefer to have the opinion of the laryngologist and the dentist. In males it is a good rule to massage the prostate and to take cultures from the prostatic secretion. In examining the joints particular attention should be paid to the location of the lesion. First, we must determine whether the joint itself is involved or whether the inflammation is in the muscles and tendons in the neighborhood

of the joint. If the joint itself is involved, is the inflammation periarticular or does it involve the bone and the articular surface? If it involves the articular surface, has the cartilage been destroyed, and what is the degree of ankylosis? Is the ankylosis fibrous or bony?

The most important laboratory tests are, first, the Wassermann; second, the determination of blood-sugar, and third, the determination of uric acid in the blood. These three tests should be made as a routine in every case. A negative Wassermann eliminates a luetic joint. The amount of blood-sugar tells us whether or not we are dealing with a low sugar tolerance, and the quantitative determination of uric acid would indicate what rôle, if any, the purin metabolism is playing in the case.

The *x*-ray is very valuable in determining how far advanced the joint lesion may be. It is, therefore, of great assistance in prognosis. Furthermore, it is very desirable to have *x*-ray photographs of all crowns and all dead teeth, as apical abscesses are readily demonstrated by this procedure.

Cultures should be taken whenever a possible focus has been discovered, not only on account of the valuable information obtained from them, but in order that the patient's own bacteria may be available in case an autogenous vaccine is desired.

In the treatment of arthritis we must first determine whether we are dealing with an active infection or with a case in which infection has already been overcome and in which the symptoms are referable to the fibrous changes subsequent to the infection. This distinction can usually be made by the appearance of the joints. In the active cases the joints are swollen, often slightly reddened, and tender on pressure. Motion is apt to be more painful in the active infections than in the healing type. In the postinfective stage the joints may or may not be enlarged, depending on the amount of newly formed fibrous tissue and bony thickening which have occurred. There is usually considerable stiffness and some pain on motion. The motion may be limited or may be entirely absent if ankylosis has occurred.

In the active cases the first indication is to remove any possible sources of infection. After this matter has been attended to, the treatment of the joint itself can be instituted. In the treatment of the joint, heat is by far the most important therapeutic measure at our command. This may be applied in different ways. Hot baths are of great value, also baking, electric pads, sun baths, etc.

The hot bath is perhaps the simplest way of applying heat to the joints. In the clinic we recommend a daily hot bath for nearly all our patients. The water should be just as hot as the patient can bear it. Baking can also be applied at home if the patient will provide himself with one of the small electric baking ovens which are now on the market. The electric pad is also very useful, but the temperature, of course, is not as high as that obtained in the baking oven. Diathermy is an ideal method of applying heat to the joint, but, unfortunately, is not available for many patients.

Massage must be used with great caution in the active cases. At a certain stage in the treatment massage should be tried and continued if no unfavorable symptoms follow its application.

Next to heat and massage the regulation of the diet is perhaps most important. As a matter of routine I recommend a low carbohydrate diet for these patients, and in the obstinate cases I try them on what amounts to a diabetic régime.

The bowels should be kept open by laxatives if necessary. In those cases that are referable to the gastro-intestinal tract high colonic irrigations are often of great value.

In the matter of drugs I occasionally use salicylates, but much more frequently potassium iodid or hydriodic acid. In the treatment of arthritis in the postinfectious stage it may still be necessary to remove some focus of infection. Otherwise there is danger of a recurrence of the arthritis. Again, heat and massage are valuable at this stage, and both active and passive exercises are very important. It is surprising how much motion can be restored to a stiff joint by the patient and long-continued use of passive movements.

Finally, we must remember that no case of arthritis is incurable as long as ankylosis can be avoided. We should also be careful about claiming too much for any one form of treatment. Arthritis, like rheumatic fever, tends to be a self-limiting disease. It is true that in neglected cases there is a tendency for the disease to recur, and after several recurrences a chronic condition may develop, but undoubtedly a considerable number of arthritics will recover from a particular attack without the administration of any therapeutic agent whatever.

CLINIC OF DR. MAURICE FISHBERG

MONTEFIORE HOSPITAL FOR CHRONIC DISEASES

THE TONSILS IN THE TUBERCULOUS

ABOUT ten years ago a tuberculous patient under my care, in whom the process in the lungs had lasted for many years but showed strong tendencies to cicatrization, told me he feels that he is getting well despite my warning to the effect that the disease is smoldering. He said that he based his opinion on the fact that he is again "subject to colds" and is suffering from acute rhinopharyngeal troubles now and then. On further inquiry he informed me that with the advent of the symptoms of tuberculosis of the lungs the tendencies to colds which he showed all his life vanished. Exposure often resulted in an increase in the intensity of the lung disease, the fever, cough, expectoration, pain in the chest, etc., but the nose and throat remained free from inflammatory phenomena. Being quite intelligent and observant he noted that during the two remissions in the tuberculous process, each lasting over two years, his proclivities to cold in the rhinopharynx returned, to disappear with the advent of the symptoms of the tuberculous lung lesion. He concluded that inasmuch as he has had three "colds" during the past two months, he felt that the activity of the tuberculous process in the lungs had abated.

This hint induced me to make inquiries along these lines, and I soon noted that during epidemics of coryza, common during the autumn and winter months, tuberculous patients are, as a rule, spared. In sanatoriums and hospitals for the tuberculous the doctors, nurses, orderlies, and the rest of the personnel are at times attacked by tonsillitis, rhinopharyngitis, coryza, etc. The introduction of one case may be effective in

spreading the malady among the personnel, and within a couple of weeks nearly all sustain more or less severe attacks of the acute infection. But among the patients, though they are in quite close contact with the doctors, nurses, and orderlies, a case is exceptional. It has also struck me as noteworthy that patients suffering from active and progressive tuberculous disease of the lungs, with fever, cough, copious expectoration, etc., hardly ever contract acute coryza or tonsillitis. Those in whom the tuberculous disease is active but not progressive may contract acute coryza or tonsillitis, but the superimposed infection runs a mild course, causing but slight symptoms. On the other hand, those in whom the lung lesion is latent or quiescent may contract coryza in a more or less acute form, the symptoms lasting several days, and followed by that slow convalescence and asthenia characteristic of tonsillitis, coryza, rhinopharyngitis, etc.

Many times making my rounds in the wards and finding that some members of the house staff or nurses suffer from acute coryza, I inquired for cases among the patients, knowing that they come in contact sufficiently close to contract the disease because it is spread by droplet infection, but I almost invariably found that the above-mentioned rule holds.

This phenomenon has also been observed in private practice. Patients with progressive tuberculosis of the lungs mingling with people in congested cities only rarely contract the acute infectious diseases of the upper respiratory tract. In a home in which an epidemic of these maladies occurs, one member of the family after another contracting the malady, the member suffering from active tuberculosis of the lungs, as a rule, escapes.

A somewhat similar phenomenon was observed during the great pandemics of influenza which we witnessed during 1918–20. In sanatoriums and hospitals for tuberculous patients the epidemic disease claimed comparatively few victims among the patients, while the personnel, the physicians, and nurses suffered to about the same degree as the population of the city or village in which the institutions were located. This phenomenon was observed at the Montefiore Hospital soon after the first epi-

demic wave had spent itself. Most of the doctors and nurses in this hospital suffered, but among the tuberculous patients those with symptoms of active tuberculosis escaped with but few exceptions. Those in whom the disease was quiescent were more liable to influenza or complicating bronchopneumonia. When I reported these observations in a paper on Influenza and Tuberculosis many objections were raised. But later on confirmation was published from institutions located in various countries. Some writers even spoke of a certain immunity to influenza enjoyed by tuberculous patients.

We now have further substantiation of these remarkable clinical phenomena. The mortality statistics for 1918–20 have now appeared in the various government reports on vital statistics. The general death-rates were frightfully high in all countries in which the epidemic disease raged during those years, but it is a noteworthy fact that the mortality in sanatoriums and hospitals for consumptives was not higher during 1918–20 than during previous years.

Some have maintained that the immunity of the tuberculous to influenza, coryza, tonsillitis, etc., is mainly due to their isolation in institutions which are well ventilated and kept scrupulously clean. However, the fact that the personnel usually is subject to these diseases during epidemics, and they come in close contact with the patients at least during the initial stages of the malady, is against the view that isolation in institutions is responsible for the immunity of the patients.

We are aware of the large number of inactive cases of tuberculosis in sanatoriums and also the so-called "suspects." In these there may be dubious signs of localized lesions in the lungs, some mild symptoms pointing to tuberculosis, but the sputum is usually scanty or lacking, and fails to reveal tubercle bacilli on microscopic examination. It is well known that the vast majority of these patients are non-tuberculous, at least in the clinical sense. And just among these colds, coryza, tonsillitis, rhinopharyngitis, influenza, grip, etc., are as common as among the non-tuberculous.

Further clinical observations have revealed the following

interesting clinical facts bearing on this subject: The tuberculous patient, as a rule, has small tonsils. Large hypertrophied tonsils are very uncommon in patients suffering from active and progressive tuberculous disease of the lungs. Altogether the mucous membrane of the upper respiratory tract in tuberculous patients is, as a rule, pale; lymphoid follicles on the back of the pharynx and adenoids are very rare. This fact has been confirmed by carefully noting the size and color of the tonsils in the numerous tuberculous patients I examined during the past ten years. In incipient cases, tending to recovery, we at times see moderately large tonsils and hypertrophied lymphoid follicles on the back of the pharynx; rarely adenoid vegetations may be discovered in the rhinopharynx, but in progressive tuberculous cases the tonsils are small, often almost absent to a degree as to suggest prior radical tonsillectomy, the pillars and posterior wall of the pharynx are pale, and no lymphoid follicles can be detected on careful inspection. Lingual tonsils and adenoid vegetation are extremely rare among the clinically tuberculous.

On the principle that observations must be checked up by several observers before they can be considered reliable, I have asked my co-workers, Doctors B. Stivelman and J. J. Wiener, to take special note on these points among the patients at the Bedford Hills Sanatorium and the Montefiore Hospital. Their reports, based on hundreds of cases, which will be published elsewhere, are to the effect that the above-mentioned observations are correct as far as the patients of these institutions are concerned.

Our wards at the Montefiore Hospital are filled with tuberculous patients in the far-advanced stages of the disease, many of them having signs of large cavities in the lungs. Of this latter class, though sick for many years, a large proportion feel quite well and appear very well nourished; some are even obese to a degree. In many of these the pleura is thickened and adherent, the heart displaced, they are breathless and cyanosed. But they are either completely afebrile or running a mild degree of fever to which they had become habituated, so that it does not materially interfere with their well being. It is among this class of

patients, who hold on in a good or fair condition despite the extensive destruction of lung tissue, that we usually find the mucous membrane of the rhinopharynx red and injected, the lymphoid follicles at the back of the throat enlarged, and the tonsils more or less hypertrophied. Conversely, when we examine the throats of patients in whom the tuberculous process in the lungs is active and progressive, who run high fever, cough and expectorate large quantities of sputum, are emaciated, and are going steadily down hill despite all efforts to save them, we find that their tonsils are small, or hardly visible, the mucous membrane of the pillars and back of the pharynx is pale, and no lymphoid follicles are seen on the posterior pharyngeal wall.

Further confirmation of these observations are found in the demographic facts, of which there is an abundance in every civilized country in which vital statistics have been published by the government. It has been shown that pulmonary tuberculosis of the chronic type is only rarely a cause of death among children under twelve years of age, though tuberculosis of the glands, bones, joints, and serous membranes, which is not often fatal, is very common, more so than in adults. At this period of life the lymphoid tissue, especially that in the rhinopharynx, is very abundant in most children. The large number of children with adenoid vegetations in the throat and with hypertrophied tonsils attest to the contention that the lymphoid tissue in children of school age is superabundant. We also know from reliable evidence gathered all over the world that at this period of life most of the infections with tubercle bacilli take place. Evidently the child's body, or at least its lungs, can resist tuberculous infection in a most remarkable manner. Infection, even if followed by disease, is localized in the bones, joints, or glands; the lungs, as a rule, remain free from active and progressive disease, except in some in which terminal caseous bronchopneumonia occurs.

When we correlate the fact that during adolescence there occurs a recession in the lymphoid tissue in the body with the just-mentioned demographic facts, our point becomes clear. After fifteen years of age the tonsils and, if present during child-

hood, adenoids, become small or almost disappear very frequently. And it is at this period of life that pulmonary tuberculosis makes its appearance; it is a disease of persons over fifteen years of age.

Investigations made during the past ten years indicate that pulmonary tuberculosis occurs most frequently in persons in whom the atrophy of the lymphoid tissue in Waldeyer's tonsillar ring is extreme. When appearing in patients in whom the tonsils are large, in whom adenoid vegetations in the rhinopharynx are prominent, and the lymphoid follicles on the back of the pharynx are large, the tuberculous process in the lungs runs a mild course and tends to recovery in the vast majority of cases.

Now and then we meet with cases of active tuberculosis with positive sputum and symptoms which leave no doubt that we are dealing with this disease. But, irrespective of the treatment applied, or even of lack of treatment, the patients do well. The fever is rather low, the pulse slow, and the general nutrition does not suffer materially. Within a month or two the cough abates or disappears, the temperature becomes normal, and the patient regains his lost weight. We then believe that there was either an erroneous diagnosis, or that we were dealing with the well-known syndrome of abortive tuberculosis. An inspection of the throat will reveal in nearly all these cases that the throat is red and injected, the tonsils large, that there is a visible lingual tonsil, and perhaps signs of adenoid vegetations. In fact, these signs may be responsible for our opinion that the case was, in fact, one of subacute rhinopharyngitis, tonsillitis, etc. But a careful examination of the chest, or a good roentgenogram, shows distinct signs of a localized apical lesion, or, more commonly, some signs of pleurisy. In fact, patients with enlarged tonsils and adenoids are known to be more liable to pleurisy than others. These mild tuberculous lesions in the lungs are liable to recurrence, and many writers have described recurrent apical pleurisy.

These patients do well as long as the tonsils and adenoids are not removed surgically. We see annually numerous cases

in which incipient, quiescent, or latent tuberculosis of the lungs had become reactivated soon after tonsillectomy. This point should be borne in mind by those who meet cases of hypertrophied tonsils showing positive or dubious symptoms and signs of inactive or quiescent tuberculous lesions in the lungs. In active tuberculous cases tonsillectomy is often followed by tuberculosis of the larynx. We have several cases of this kind admitted to the Montefiore Hospital annually. These patients were tuberculous, but got along well or fairly well. A laryngologist then decided that the cough is due to the large tonsils or to the adenoids, and removed these glands. Ever since the symptoms became more acute and progressive, hoarseness and dysphagia were not tardy in making their appearance, and the end is near.

In contrast with these cases we observe passing through our wards that patients with active and progressive tuberculosis of the lungs have pale throats, small tonsils, only rarely is the lingual tonsil visible, in fact, the sinus tonsillaris appears excavated, suggestive of prior radical tonsillectomy. I have often asked these patients whether they had their tonsils removed surgically because of the appearance of the sinus tonsillaris. Dr. Danziger, whose experience in laryngeal tuberculosis has been immense, has confirmed these observations. In fact, it may be stated that it is rare to find large tonsils in patients suffering from laryngeal tuberculosis; the reverse is the rule.

The condition of the lymphoid tissue in the throat is, within certain limits, a good indicator of prognostic significance. In the vast majority of cases of active tuberculosis the prognosis is unfavorable when the tonsils are small, the mucous membrane of the rhinopharynx pale, and no lymphoid follicles can be seen on inspection of the throat. The prognosis is good in tuberculous patients with large tonsils, adenoid vegetations, and congested mucous membrane. Tuberculous patients who contract coryza, tonsillitis, and rhinopharyngitis, especially of the epidemic type, have a better outlook than those who escape these maladies when exposed to infections.

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EARLY DIAGNOSIS OF TUBERCULOSIS

THE recent fall in the death-rate of pulmonary tuberculosis is being attributed by various observers to many causes. A great number have explained this decrease in death-rate by the recent influenza epidemic. The epidemic carried off a large number of cases of pulmonary tuberculosis which, if alive at the present time, would keep up the death-rate of previous years. That the influenza epidemic accounted for some of the decrease in the death-rate cannot be denied, but perhaps some of the decrease may also be due to a better understanding of the means of diagnosis of the incipient form of pulmonary tuberculosis. A few years ago the incipient form of pulmonary tuberculosis, as a rule, was overlooked. The number of cases in which the best results could be obtained with simple treatment came to the doctor ro to the sanitarium when it was almost too late.

A diagnosis of incipient tuberculosis is, with few exceptions, a cure. Therefore, may not this concerted action of the medical schools, organizations, and individual workers in teaching better methods of diagnosis have brought forth a considerably greater number of cases of the incipient form of tuberculosis of the lungs?

An early diagnosis can mean only a lower death-rate. The early diagnosis, unfortunately, does not depend solely on a careful history, or on a thorough physical examination, or on a Roentgen ray interpretation from an experienced roentgenologist, or even on the complement-fixation test by the laboratory diagnostician. Throughout the literature one reads of how the

clinician, the roentgenologist, and the laboratory worker have been the chief means of diagnosis of this important group of cases of pulmonary tuberculosis. Experience has shown that only a combination of history, physical examination, Roentgen ray interpretation, and laboratory determination may be necessary to make the diagnosis. In one case the history may play the important rôle; in another case the physical examination or the *x*-ray may be the deciding factor.

Therefore it is important to know how to write a good history to bring forth the important physical findings and to interpret a good roentgenogram. Inasmuch as the interpretation of *x*-rays dealing with incipient tuberculosis is of value only in the hands of an experienced roentgenologist, attention should be centered on the taking of the history, which can be easily taught, and on the physical findings, with which we are well acquainted, but perhaps are not familiar with the procedure for bringing them forth.

History.—The question of history writing in diseases of the lung is of utmost importance. From a good history not only is a lead to the diagnosis obtained, but also the facts on which the determination of the activity of the disease is based. One would think that a history should be the story of why the patient came to the doctor. Unfortunately, in insidious diseases of the lungs, the symptoms vary so little from the normal that, unless special stress is laid upon them, the patient does not mention them to the physician.

For example, a patient may say that she has had a cold for the last few years, when she really means that for the last few years she has had a cough. The cough has never been severe enough to bother her except for short periods. The morning expectoration meant nothing because it was supposed to be the natural accumulation of mucus in the nasopharynx after a night's sleep. The acute exacerbations were the so-called frequent colds. Questioned at first if there was a cough, the reply would be "*No.*" The slight cough, morning and night, meant nothing to the patient. Only after asking "*Do you cough at all, particularly in the morning?*" do you get the answer, "*Yes, I*

have a little irritation in the throat, and cough for a few minutes in the morning." Therefore, after listening to the patient's complaints and when they tend to point to a disease of the lungs, the following history must be elicited:

(1) The question of toxemia is determined because, depending on whether or not the patient shows evidences of toxemia, is the condition made a clinical one. The symptoms of toxemia are the same for every disease: the general feeling of debility, nerve irritability, digestive disturbances, dyspnea on exertion, rapid pulse, fever, night-sweats, sleeplessness, headaches, and loss of weight. They are, as a rule, not all present. The important symptoms are temperature and pulse. Do not be content to call "normal" slight increases in temperature and pulse-rate for long periods of time. They are not normal. We must account for these increases by other factors. Innumerable causes may be given for such increases. It is not the object of this clinic to give the causes of an increase in temperature and pulse. If the causes you give, after being eliminated, have no effect on the decline of the temperature and pulse-rate, begin to think of tuberculosis. The same may be said for the other signs of toxemia. They must be explained, and we must remember that pulmonary tuberculosis may very easily be responsible for them. With a long history of toxemia, tuberculosis must at once be thought of.

(2) Pathologic lesions in the lungs produce a group of reflex symptoms. These reflex symptoms do not mean pulmonary tuberculosis, but they do mean pathology in the lung. Therefore, it is essential that we be familiar with this group of symptoms.

Pottenger[1] has laid considerable stress upon them. He groups them as follows:

Hoarseness.
Tickling in the larynx.
Cough.

[1] F. M. Pottenger, A Discussion of the Classification of Pulmonary Tuberculosis, American Review of Tuberculosis, October, 1922, Vol. 6, No. 8.

Circulatory disturbances.
Chest and shoulder pains.
Spasm of muscles of shoulder-girdle.
Digestive disturbances (hypermotility and hypersecretion).
Flushing of the face.

The above may occur with any pathologic condition in the lungs. Inasmuch as pulmonary tuberculosis is the most frequent infection involving the lungs, it is the one most often responsible for reflex symptoms. Is it not common for the nose and throat specialist to send the tuberculous patient to the internist? Does not the tuberculous patient frequently go to the gastro-enterologist for relief for the gastric disturbances? Does not the same patient go to the doctor for the vague pains in the shoulder and chest? The reflex irritabilities, particularly when there is no pathologic condition to account for them, must be associated with some abnormal condition of the lungs. This brings forth another group of symptoms, symptoms of utmost importance, due to the lesion of the lung *per se*. These are expectoration, hemoptysis, and pleurisy with effusion. The expectoration is always associated with the reflex symptom—cough. Expectoration may occur in other conditions, but its existence over a long period of time must make one suspicious of tuberculous involvement of the lungs. It is very easy to have the sputum examined frequently. One negative sputum means nothing. A series of negative sputums may make one doubtful, but never can they mean a non-tuberculous involvement. Only a positive sputum is of importance.

(3) The coughing up of blood is almost pathognomonic of the disease. The amount must be at least a dram or more. Any sign of blood from the lungs, however, should be considered as due to a pulmonary tuberculosis until proved otherwise. It may occur in other conditions, as, for example, in mitral stenosis, pneumonoconiosis, and probably in syphilis of the lung. The latter three conditions, however, are not as frequently seen as tuberculosis. They occur only occasionally and, consequently, a diagnosis of tuberculosis should be made on the occurrence of hemoptysis until it can be explained on another pathologic basis.

The same is true for pleurisy with effusion. From experience we know it is almost always associated with a tuberculous process, although it may occur with other conditions, particularly with malignant tumors and unresolved pneumonias. Therefore a history of wet pleurisy should be considered as due to a tuberculous infection until proved otherwise.

In summing up the history we have three groups of symptoms: the first being the toxic, on which the activity of the disease is based; the second, the reflex, which points to a pathologic condition in the lungs; and the third, due to the process in the lungs, which is almost pathognomonic of the disease. It is surprising how often, even in the minimal lesion, the history of hemoptysis and wet pleurisies can be elicited.

Physical Examination.—The success of the physical examination is dependent on the ability of the examiner to elicit the physical findings and then to interpret them. We will center our attention first on the procedure of the examination and later on the interpretation of the findings. Remember that, as in history taking, the changes may be only slightly different from the normal, and unless keenly sought for they may be overlooked. As we are dealing with incipient forms of the disease, inspection and palpation are not of great assistance. Muscle spasm, diminished expansion, etc., may be present, but only those clinicians with long experience in these methods are able to pick up the above findings. We must depend, then, chiefly on percussion and auscultation in the examination.

Procedure of Examination.—The patient is seated comfortably on a backless, revolving chair. The examiner is also made comfortable so that he may give his undivided attention to the patient. Percussion of the chest is made from the base to the apex. In this way we go from the normal to the pathologic area, as tuberculosis only rarely invades the base primarily. Comparison of the right side with the left may lead one astray, as a bilateral involvement of the upper lobes of both lungs is very common. Light percussion is the choice, as heavy percussion sets larger areas of the lung in vibration and a small area of infiltration may be overlooked.

In auscultation the patient is instructed to breathe normally through the mouth. Forced breathing will exaggerate breath sounds. A prolonged expiration can easily be produced by forced breathing. The intensity of the breath sounds may seem normal with forced breathing, and yet be greatly diminished with normal breathing. Therefore, it is important at first to listen to the breath sounds under normal conditions, and then, if one wishes to accentuate any of the breath sounds, the patient is told to breathe correspondingly deeply. In listening to breath sounds attention must be given not only to the quality, pitch, and the intensity of the sounds but also to their relationship to the inspiratory and expiratory movements of the chest. There has been very little emphasis placed on the latter. We must remember that in vesicular breathing the sound heard during the act of inspiration begins and ends with inspiration. In bronchial breathing the sound begins with, but does not finish with, inspiration, and in emphysematous breathing it starts after the beginning of inspiration, but continues throughout the act. The same method of procedure is carried out as under percussion (examination from base to apex). Any modifications of the normal breath sounds or adventitious sounds are noted. If no râles are heard with normal breathing, they may be brought out, if present, in the following manner: The patient is told to exhale, cough gently, and then to breathe deeply. This procedure will bring out râles if they are present, and accentuate râles heard during normal breathing. Râles produced in this manner are called latent râles.

One may ask, What are the signs of incipient pulmonary tuberculosis? Are they different from the signs heard in other pathologic lung conditions? The question may be answered by saying that the signs for all pathologic diseases are the same. Surely an infiltration of the parenchyma of the lungs by cancer cells, tubercle bacilli, or by a dust particle will produce the same physical findings. They will bring forth bronchovesicular breathing and perhaps râles. Dulness on percussion may be present in the three conditions. Then on what, one asks, can we base our diagnosis?

Fortunately, various forms of infections have a predilection for various regions of the lung. Tuberculosis attacks the upper lobes and rarely does it primarily occur at the base. Therefore, we may state that modifications of the normal breath sounds and adventitious sounds heard above the third rib anteriorly and the fourth vertebral spine posteriorly should be considered as a tuberculous process until they can be accounted for by another condition. Changes occurring at the base of the lungs are to be considered as non-tuberculous until proved to be tuberculous.

The most constant findings are bronchovesicular breathing and impairment of resonance on percussion. Râles, when present, are pathognomonic of the disease. Unfortunately, however, râles are not always present, whereas, due to the infiltrative processes of the infection, bronchovesicular breathing is almost always present. The amount of bronchial element in the bronchovesicular breathing is almost proportionate to the amount of infiltration. The râles, as a rule, are moist and mucous in character, but may be of any character except sonorous or sibilant. Creaks, clicks, or other indeterminate râles heard in the upper lobes must be regarded as due to tuberculosis.

As important as the location of the râles is their persistence. The pitch of the râles is dependent upon the surrounding tissue and, therefore, in tuberculous infiltration they are high in pitch. Diminished intensity of the breath sounds may be associated with peribronchial tuberculosis. Here the caliber of the bronchial tube is diminished and less air gets to the part of the lung supplied by that bronchus. Diminished breath sounds may also be due to a thickened pleura, which is a frequent accompaniment to tuberculous infiltration. Inasmuch as the changes in breath sounds vary so little from the normal in so many cases, there is apt to be some confusion with the bronchovesicular breathing heard normally in the chest, as, for example, the right apex and posteriorly below the angle of the left scapula. When bronchovesicular breathing is heard in these regions one may hesitate calling them abnormal. That some bronchial element is heard with the vesicular sound in these normal regions cannot be denied. I think that the breath sound heard at the right

apex should be termed "vesiculobronchial," inasmuch as the bronchial element is very small in comparison to the vesicular. It is safer to call bronchovesicular breathing at the right apex and check up the findings with an *x*-ray, than it is to call bronchovesicular breathing due to a parenchymatous infiltration a normal condition. Many an incipient tuberculosis is overlooked because bronchovesicular breathing at the right apex is thought to be always normal.

It is seen from the above that the character of the physical findings is not as important as the situation of these physical findings. Physical findings indicating infiltration in the upper lobes must be considered as tuberculous until accounted for by other pathologic conditions.

The following cases will demonstrate how the history, the physical examination, and the *x*-ray take the dominant rôles in the diagnosis.

Case I.—I. L., married housewife, came to this clinic August 12, 1922, complaining of cough and expectoration that had been present since the onset of her present illness, December, 1920. The cough and expectoration are increased in the morning upon arising and at night when retiring. She has lost 21¾ pounds in one year. She is easily tired, becomes dyspneic on exertion, and sleeps restlessly because of night-sweats. Her appetite is very poor, having almost no desire for food. For short periods of time she has had pain in the right shoulder. In December, 1920 she had a hemoptysis (half a glass of bright blood). Her temperature is 99° F. and her pulse-rate 120. Family and previous history are irrelevant.

Physical Examination.—Examination disclosed dulness over the right upper lobe anteriorly down to the second rib and posteriorly to the fourth vertebral spine. Bronchovesicular breathing and moist mucous râles are heard in the same region. Her sputum was reported positive for tubercle bacilli on August 15, 1922.

Discussion.—There is everything in this case that points to a pulmonary tuberculosis. The history is almost decisive. The physical examination with the history makes a definite

diagnosis of pulmonary tuberculosis, which the positive sputum examination confirmed. This case is interesting in that the history gives all the symptoms of toxemia, reflex irritation, and of the lesion *per se*.

Toxemia.....	Night-sweats, Loss of weight, Dyspnea, Loss of appetite, Temperature 99° F., Pulse 120.
Reflex.....	Cough, Hoarseness, Pain in right shoulder.
Lesion *per se*	Hemoptysis, Expectoration.

Case II.—G. B., male, white, aged twenty years. His chief complaint is that he has had a blood-streaked sputum for the last week. He coughs slightly, with little expectoration. Two years previously he had a blood-streaked sputum for about a week. Otherwise he is in good physical condition. There is no loss of weight. He eats and sleeps well. He came to the clinic because of the blood in the sputum. His temperature is 98° F., his pulse-rate is 96, the respiration 24. Previous and family history are irrelevant.

Physical Examination.—The right lung: There is dulness on percussion to the third rib anteriorly and the third vertebral spine posteriorly. Bronchovesicular breathing is heard in the same region. A few fine mucous râles are heard in the first interspace after cough. *The left lung:* There is dulness on percussion to the second rib anteriorly. The breath sounds throughout the lung are normal. A few fine mucous râles are heard over the clavicle after coughing. Sputum examination was positive.

Stereoscopic roentgenograms disclose the following: *Right lung:* Root shadows are exaggerated, with infiltration of descending bronchial trunks, and thickening of the vertebral

trunk to the apex. No parenchymatous lesion is present. *Left lung:* Root shadows are greatly exaggerated and extend into the parenchyma of the lung. Small areas of calcification are present in the root region. A parenchymatous infiltration is seen down

Fig. 118.—Case II.

to the second rib anteriorly and the fourth vertebral spine posteriorly. Apical pleurisy is present. There is an annular shadow in the circle of the first rib. There is tenting of the left diaphragm in its outer third.

Discussion.—This case is striking in that the patient has shown so few symptoms in the last two years. If it were not for the blood-streaked sputum he probably would not have consulted a physician. The comparison of the physical findings and the *x*-ray is also very interesting, inasmuch as from the physical examination the lesion appears to be chiefly on the right side, whereas the *x*-ray shows a definite lesion on the left side and a questionable one on the right. If no positive sputum were present, there is no question that the diagnosis would rest, in this case, entirely on the *x*-ray examination.

Case III.—J. D., female, white, married, thirty years of age, came to the clinic on September 15, 1922. Her chief complaint was cough. The cough began six months previously. It is dry in character and accompanied by scanty expectoration. Along with this cough and expectoration the patient gradually lost her voice and has been hoarse the last few months. In the last few weeks all her symptoms have become aggravated. She also feels tired and sleeps restlessly on account of night-sweats. Her appetite is very poor. She is troubled with constipation. For the last few weeks she has been complaining of vague pains in her left shoulder-girdle. The previous and family history are of no importance.

Physical Examination.—Right lung: There is no impairment of resonance on percussion. Diminished breath sounds are heard over the upper right lobe. No râles are heard, even after coughing. *Left lung:* Dulness on percussion is heard anteriorly to the third rib and posteriorly to fifth vertebral spine. Bronchovesicular breathing, diminished in intensity, is heard from the apex to the third rib.

Moist mucous râles are heard in the fourth interspace close to the axilla. Posteriorly bronchovesicular breathing and moist râles are heard down to fourth vertebral spine.

x-Ray examination of the chest reveals—Right lung: The root shadows are exaggerated. There is an infiltration of the descending bronchial trunks. *Left lung:* The root shadows are exaggerated and extend into the parenchyma of the lung. There

is a parenchymatous infiltration down to the third rib and sixth vertebral spine. There is an annular shadow in the first interspace. A thickened pleura extends from the apex to the third rib anteriorly.

Fig. 119.—Case III.

Sputum reported positive for tubercle bacilli on September 29, 1922.

Discussion.—This case is presented to demonstrate how the history may point to an involvement of the lungs. We see a

combination of symptoms due to toxemia and reflex lung irritability. From the history a diagnosis of tuberculosis cannot be made, but it nevertheless points to a toxemia probably caused by an infection of the lungs. The physical examination made the diagnosis positive, which again the sputum examination confirmed. The *x*-ray was not necessary for a diagnosis. It was only of value as a record of the extent and character of the lesion.

Case IV.—W. B., white male, twenty years of age, and single, came to the clinic as a "tuberculous contact." His mother recently died of pulmonary tuberculosis. Except for being underweight, he has had nothing to complain of. If the visiting nurse had not insisted on his coming to the clinic he would not have consulted a physician. On examination his temperature was normal, his pulse-rate 96, and respirations were 24 per minute. He said he enjoyed perfect health except for his being under weight.

Physical Examination.—Right lung: Percussion shows dulness to the second rib anteriorly and the fourth vertebral spine posteriorly. Bronchovesicular breathing in these regions. Moist râles are heard after coughing from the apex to the second rib. *Left lung:* Negative for abnormal physical finding.

x-Ray.—Right lung: The root shadows are slightly exaggerated. Anteriorly there is a parenchymatous infiltration from the first to the fourth ribs, and posteriorly from the apex to the sixth vertebral spine. An annular shadow is seen anteriorly between the lower margin of the second rib and the upper margin of the third rib. *Left lung:* The root shadows extend into the parenchyma of the lung. No parenchymatous infiltration present.

Discussion.—This case is interesting in that we have a little more than an incipient case of tuberculosis and no history of any sort. Furthermore, the physical findings occur in the region of the chest where similar signs are to be found under normal conditions. Fortunately, râles are heard in this case and there is less chance to err. With no history of any discomfort and only bronchovesicular breathing in the right upper

lobe, one would naturally hesitate to make a diagnosis. This is the type of case in which the Roentgen ray plays the dominant rôle. It is interesting to note that the patient later showed an

Fig. 120.—Case IV.

afternoon rise of temperature and increase in pulse. His sputum examinations were all negative for tubercle bacilli.

Case V.—M. H., white male, South American, thirty-two years of age, a tailor by occupation, came to the clinic August

7, 1922. He was referred to the clinic by the New York Tuberculosis Association. He complains chiefly of cough accompanied by expectoration. The cough is not annoying, but worries the patient by its persistence. Seven months ago he coughed up an ounce of blood and had a blood-streaked sputum for a week. The hemoptysis with the persistent cough made him suspicious of a possible tuberculous process. He therefore applied to the New York Tuberculosis Association, who referred him to this clinic. He also complains of pains in the lower muscles of his back. His previous history discloses a gonorrheal infection at seventeen, and he also thought he might have had a primary specific lesion. His temperature and pulse-rate are normal.

Physical Examination.—Right lung: Percussion shows impairment of resonance to the second rib anteriorly and the fourth vertebral spine posteriorly. The breath sounds are diminished in intensity in these regions. Posteriorly from the eighth vertebral spine to the base moist mucous râles are heard. *Left lung:* Normal breath sounds are heard throughout; no abnormal physical findings.

x-Ray examination discloses a bilateral infiltration of the root regions and the descending bronchial trunks. Particularly are the descending trunks at the right side accentuated. They appear as a beginning form of cylindric bronchiectasis. There is no evidence of a parenchymatous infiltration of the lungs.

Discussion.—The previous history of hemoptysis should always lead to a suspicion of pulmonary tuberculosis. The findings in this case are very scanty and give little support for or against a tuberculous process. Repeated sputum examinations were negative. The *x*-ray examination excludes a tuberculous involvement of the lungs. How may we explain the hemoptysis? I have recently seen several cases giving a history of hemoptysis which, on physical examination, gave scanty and doubtful physical signs in the lungs. After the return of the report of a Wassermann the diagnosis was still further confused. Tuberculosis of the lungs in these cases was ruled out by the Roentgen picture. They all had one thing in common, a fibrotic infiltra-

tion of each hilum and of the descending bronchial trunks. May we not be dealing with a luetic infiltration of the bronchial trunks? It is interesting to note that this patient also has a

Fig. 121.—Case V.

four plus Wassermann reaction. He is having the routine treatment for syphilis and it will be interesting to note if any changes will take place in the bronchial shadows in an *x*-ray picture a few months hence.

Case VI.—Patient a white female, married, twenty-four years of age, came to the clinic on September 1, 1922. The onset of her disease dates back four years. At that time she had an attack of influenza complicated by pneumonia. After her

Fig. 122.—Case VI.

pneumonia she had a pleurisy with effusion at the right side, and a week later was operated on for an empyema. Since then she has never felt well. She tires easily, has little desire for food, and has gradually and slowly lost weight, which loss at the

end of four years amounts to 10 pounds. Four years ago she developed a cough with scanty expectoration. The cough and expectoration plus the loss of weight brought her to the clinic. Temperature and pulse-rate are normal.

Physical Examination.—Right lung: Normal breath sounds are heard throughout the lung, but diminished in intensity at the base and posteriorly over the upper lobe. *Left lung:* The intensity of the breath sounds is diminished over the upper lobe.

Sputum examination has been negative for tubercle bacilli.

x-Ray.—Right lung: Root shadows extend into the parenchyma of the lung. Fibrotic infiltration of the descending bronchial trunks, and there are deposits of cacilum here and there along their course to the diaphragm. The diaphragm is flat, with small areas of tenting. The east and phrenic angle is obliterated. No parenchymatous infiltration is seen. *Left lung:* Root shadows are exaggerated. There is a peribronchial infiltration of vertebral trunk to the apex. No parenchymatous lesion is seen.

Discussion.—This case is interesting because of the history of wet pleurisy. It was considered a case of tuberculosis until the *x*-ray excluded the disease. The *x*-ray shows that we are dealing with an infiltration of the descending bronchial trunks associated with a diaphragmatic pleurisy secondary to the pulmonic process and empyema.

CONTRIBUTION BY DR. WALTER M. KRAUS

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BRAIN TUMORS AS THE CAUSE OF SIMPLE HEMIPLEGIA

IN the course of the routine work of a general practitioner or neurologist hemiplegia plays a prominent part.

The majority of cases are due to a vascular accident, hemorrhage, thrombosis, or embolism occurring in the region of the basal motor ganglia and the internal capsule. In the minority group there are many types not only as to cause, but as to the various associated signs and symptoms. Of these, the syndromes of Weber and Millard-Gubler are well known. Furthermore, hemiplegia associated with signs of intracranial hypertension, due to a varying degree of block in some part of the cerebrospinal fluid system, is fairly common, but the associated choked disk, nausea, vomiting, and headache should render the diagnosis simple. Brain tumors causing hemiplegias associated with Jacksonian epileptic attacks in the paralyzed parts are not uncommon. The association of these spasmodic attacks with paralysis should also point the way to a diagnosis of brain tumor of the motor cortex or of subcortical areas irritatin g the motor cortex by pressure or invasion.

This discussion deals with none of these, but with a very small group of cases in which there occurs with more or less suddenness paralysis of the face, arm, and leg on one side. This hemiparalysis or hemiplegia is unassociated with any clinical evidence of increased intracranial pressure and is not complicated by convulsive seizures (Jacksonian epilepsy).

Oppenheim,[1] in discussing tumors of the motor zones, remarks: "The tumor may remain latent for a long time, and may, as the result of a hemorrhage within it or of a softening in its neighborhood, suddenly give rise to symptoms of paralysis *not preceded by* any symptoms of irritation. . . . The focal symptoms may be absent for a long time or even altogether. But as the internal capsule is usually affected, either directly or from the pressure, symptoms of ***hemiplegia*** are apt to appear. These are not, as a rule, sudden in their onset, but develop gradually and incompletely. According to my experience the 'distant effects' of the lesion on the motor tract first becomes apparent in the facial nerve and in the changes of the reflex excitability which correspond to those of a pyramidal lesion."

The following case illustrates the clinical picture produced by such tumors:

Case Report—H. H.—The patient was injured on September 2, 1921 by having his left hand squeezed between two large packing cases. When asked to point to the place injured the patient indicated the line of the metacarpophalangeal joints, in other words, the hand above the beginning of the fingers.

On December 12, 1921 the patient noticed that he had trouble in using his left leg. He states that he was dizzy and "felt badly." His family noticed that he had a paralysis of the left face, arm, and leg. Otherwise the history was negative.

Physical Examination.—The patient is unable to move his fingers. There are, however, no sensory changes. There is moderate atrophy of the small muscles of the hand as well as of the muscles of the forearm. The cranial nerves are negative beyond the slight facial palsy noted below.

The patient presents the picture of the residua of a left hemiplegia. The arm is paralyzed and hangs fairly limply at the side, slightly bent at the elbow. The leg is held stiffly and is not normally used in walking. The patient is, however, able to stand and walk. There is very slight left facial weakness which is limited to the lower half of the face. There is some difficulty in closing the left eye.

[1]Oppenheim, Text-book of Nervous Diseases, vol. 2, pages 897, 902, 1911.

The deep reflexes are exaggerated on the left side, while the abdominals are slightly diminished. No Babinski or clonus. There are no sensory changes.

Discussion.—An injury occurring in the hand could not possibly have injured the nerves to any muscles but those of the hand. It is improbable that any injury to them was caused by the accident.

At the time it was my opinion that the patient suffered a closure, thrombosis, in the right hemisphere. The location of this was either subcortical or capsular, and involved the fibers for the arm more than those for the face and leg. This injury to the brain was unquestionably an intercurrent affair and not resultant upon the original accident in any way. On the other hand, the accident was due to weakness resulting from the progressive paralysis of the arm.

Progress (January 11, 1922).—Since the original examination the patient has shown a clearly defined left hemiplegia, more pronounced than when first seen. There has been slight confusion, memory for recent events being poor. Spinal fluid entirely negative. Blood-pressure 150/86.

February 1, 1922: The patient's condition has become worse in the last few weeks. He has been stuporous most of the time. A Babinski sign is now present in the right foot. The patient has some difficulty in eating.

February 20, 1922: The condition is the same as on February 1st.

February 22, 1922: The patient died.

Autopsy revealed a tumor-like formation lying in the right cerebral hemisphere. On section, the growth was about the size of an orange and was centrally softened.

Microscopic examination showed the presence of a glioma. At the periphery of the tumor were numbers of thrombosed blood-vessels and the central portions were necrotic.[1]

Discussion.—Throughout the course of the illness of this

[1] Autopsy report of Dr. Douglas Symmers, Director of the Pathological Laboratory, Bellevue Hospital, New York City. From the service of the Chief Medical Examiner of the City of New York, Dr. Charles Norris.

patient there were no convulsive seizures of any kind. There was no evidence of any degree of block of the flow of the spinal fluid. The fundi were repeatedly examined and never showed any evidence of choking. The spinal fluid was negative. The slight atrophy of the muscles of the left hand aroused a suspicion of tumor, since such atrophies are fairly common in tumors involving the regions beneath the cortex and the adjacent basal ganglia. The appearance of a Babinski on the right side indicated pressure on the left hemisphere, which could well have been produced by swelling of the right hemisphere due to hemorrhage within it. The increasing stupor is a common symptom of cerebral hemorrhage and thrombosis.

The progress of the case is interesting in so far as it began in the arm, a not uncommon beginning of hemiplegias due to vascular accident in the subcortical region. There are not a few cases of brain tumor which begin with monoplegia and subsequently develop hemiplegia, but cases which remain at this stage and never show any other focal symptoms or any evidence of cerebrospinal fluid block are extremely uncommon.

The only suggestion which can be made for the diagnosis of a brain tumor in such patients presenting so simple a picture as that just described is the presence of the atrophy of the small muscles of the hand. This evidence is too slight to warrant a definite diagnosis in the absence of other signs or symptoms indicating brain tumor.

I wish to express my thanks to Dr. Douglas Symmers for the pathologic report of this case and to Dr. Charles Norris for his permission to publish that report.

CLINIC OF DR. A. S. BLUMGARTEN

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COMMON PITUITARY SYNDROMES

I. **Two Cases of Pituitary Tumor:** (*a*) *Pituitary Tumor in an Old Endocrinopathy.*
(*b*) *Pituitary Tumor in a Child.*
II. **Functional Pituitary Syndrome and Its Differential Diagnosis from Common Abdominal Diseases.**

I. TWO CASES OF PITUITARY TUMOR

THE work of Cushing in emphasizing the clinical syndromes of pituitary tumors is one of the outstanding accomplishments of endocrinology. The recognition of pituitary tumors is not difficult when the possibility or probability of this condition is borne in mind. The frequency, however, with which a symptomatology referable to other viscera masks for a long time the underlying pituitary origin prompts the presentation of the following cases.

The majority of the cases of pituitary tumor rarely present themselves at first to the internist interested in endocrinology. They usually complain of disturbances in other viscera, and it is not until therapy of the dominant symptoms has been unsuccessful or the development of persistent eye symptoms occurs that a pituitary tumor as a basic cause for the symptoms is suspected.

In my experience the majority of pituitary tumors first present themselves to the gynecologist for functional amenorrhea, or are treated for a long time for inexplicable vomiting or gastric

[1] From the Endocrine Clinic.

symptoms on the basis of an ulcer or a functional gastric neurosis. Many of the patients are treated for various types of headaches. When eye symptoms develop or when the ophthalmologist is asked to examine the patient to explain the headache it is then only that the serious nature of the illness is recognized.

We may divide the symptoms of pituitary tumor into two groups:

1. Symptoms of intrasellar pressure:

2. Symptoms indicative of disturbance in the endocrine function of the pituitary.

The symptoms of intrasellar pressure are usually headache, vomiting, and evidence (both subjective and objective) of pressure in the region of the optic chiasm. The headache is usually periodic, is situated in the temporal or supra-orbital regions, and but rarely on the top of the head. The headache gets progressively worse. It may be intensified before, during, or after menstruation; it is very resistant to therapy, and finally it becomes boring or throbbing in character. This headache soon becomes associated with vomiting, which may be of the projectile type, and may occur during the night when the patient is asleep. In the first stages of the disease there may be no real vomiting, but attacks of abdominal cramps or sudden attacks of nausea or abdominal distention. The headache and vomiting simply indicate an increase of the intrasellar contents and are merely evidences of mechanical pressure within the sella. The eye symptoms, which are the definite focal symptoms, may be of several kinds. Although it is generally believed that a bitemporal hemianopsia is the usual eye-picture of a pituitary tumor, this is not always the case. In many instances there may be a papilledema or engorged retinal veins, which are more apt to be one-sided, especially in the beginning, and finally an atrophy of one or the other of the optic nerves. An *x*-ray examination of the skull usually shows an erosion of the sella turcica.

The symptoms referable to the endocrine function of the pituitary are very variable because, apparently, the pituitary

gland is important in various functions of the body. Practically we see evidences of the following disturbances:

1. Disturbances in genital function.
2. Disturbances in bony growth.
3. Disturbances in carbohydrate metabolism.
4. Disturbances in salt and water metabolism.

The disturbance in the function of the genitals, which is more commonly seen in female than in male patients, usually consists of a progressive amenorrhea which is at first relative and finally complete or permanent. In male patients as well as in females there may be a progressive sterility.

The amenorrhea is usually one of the first symptoms that calls the patient's attention to any trouble. Consequently these patients are treated for a long time by the gynecologist in the hope of establishing a menstrual flow, and after six or eight months or longer of treatment, when serious eye trouble has developed, the real origin of the condition is suspected. The same is true for sterility in the males. These patients are treated for sterility long before any eye symptoms or headache develop.

The disturbances in bony growth are usually of a mild character. They usually consist of thickening of the supra-orbital ridges, or the patient may notice that the hands or feet are becoming larger. In some instances a definite picture of acromegaly develops.

Disturbances of carbohydrate metabolism in pituitary disease are usually confined to the development of an adiposity. On laboratory examination an increased sugar tolerance can also be established. The adiposity is usually confined to the epigastric or lower abdominal regions and to the thighs.

Disturbances in salt and water metabolism are usually those of a diabetes insipidus, with an excessive thirst and polyuria.

Extreme drowsiness and dizziness is a frequent occurrence in pituitary tumors, and occasionally epileptiform convulsions. In actual practice the most common combination of symptoms that we see is a syndrome of amenorrhea or sterility, pituitary headache, periodic nausea and vomiting, with a development of

adiposity and focal eye symptoms. The rarer type is the periodic headache with vomiting, the stimulation of bony growth, and amenorrhea or sterility.

Prognosis and Treatment.—The eye symptoms of pituitary tumors are the most vital. Since the patients if untreated may become permanently blind, it is essential to recognize the condition as soon as possible and to institute surgical therapy by a surgeon experienced in this kind of work. However, in many instances the patients are seen when a unilateral optic nerve has already developed and the chance of saving the eyesight is remote.

The majority of the pituitary tumors are benign and the disease progresses until erosion of the sella turcica takes place, when the pituitary headaches are relieved. The indication for operation is usually the eye symptoms. If the eye symptoms are progressive, surgical interference is imperative. If, however, the process has come to a standstill and has left the patient without headaches, but with a unilateral optic nerve atrophy, it is often advisable to let him alone, as there is nothing to be gained by surgical interference, and practically the patient is just as well off with a permanent optic nerve atrophy, providing there is no progress of the lesion. *x*-Ray or radium therapy is very useful following operative procedures.

Case I.—Pituitary Tumor Developing in an Old Endocrinopathy.—P. B., a married woman of thirty-seven, was referred to the Endocrine Clinic in September, 1922, complaining chiefly of headaches, ringing in the ears, and eye symptoms. The illness began about three years ago with a sensation of dizziness confined to the supra-orbital regions and associated with diplopia and headaches. The dizziness and headaches were periodic and would occur about every three to six months. The attacks begin with a sensation of dizziness, blurring of vision, and are followed in about fifteen minutes to an hour by headaches. The headaches begin in the supra-orbital region, extend along the temporal regions to the ears, then all over the head and into the bridge of the nose. This is usually associated with an

attack of intense nausea, but no vomiting. When she lies down the headaches usually occur in association with an attack of belching of gas. She has developed constant ringing in the ears. There has been no change in her weight and she perspires slightly. The attacks are usually followed by a sensation of dulness and fulness in the head. During the last few months the attacks have increased in frequency and they have become more intense. She has also noticed lately that her hands have been growing larger and that her vision has been getting somewhat worse.

Past History.—She does not remember having any of the usual children's illnesses except typhus. She had an attack of grip about a year ago. She has had four nasal operations during the last four years in an effort to relieve her headaches, and although she has been able to breathe somewhat better since the first operation the operations have made no impression at all on her headaches.

Menstrual History.—She has never menstruated, and about once in a great while she has a slight expectoration of blood not associated with cough. She has been told that she has not been developed. She has been married fourteen years and has had no children.

Habits.—She has no special desire for any kind of food. She does not eat rye bread because it produces a full sensation in the epigastrium, and she has given up eating potatoes because they have a tendency to develop gas. She does not drink much water.

Family History.—Her father died about fourteen years ago, at the age of sixty-four; she does not remember the cause. He was about the same height as the patient, and not stout. He had good health.

Her mother died about the same time as her father, at the age of sixty-three; she had rheumatism; she was a very stout woman and died suddenly of heart trouble.

The patient has 4 sisters and 1 brother. They are all married, most of them are short and of medium stature, and very prolific. They have from 4 to 9 children apiece.

Examination shows the following:

Measurements

Weight	155 pounds
Height	63½ inches
Span	69 "
Lower extremities	33½ "
Torso	30 "
Circumference of head	22 "
Circumference of neck	14 "
Width of shoulders	16 "
Circumference of chest	35 "
Circumference of waist	30½ "
Circumference of abdomen (maximum)	37½ "
Circumference of buttocks	39½ "
Pulse	80
Blood-pressure	120/80

Description.—A rather tall, broad-featured, bony, gorilla-like woman. The skin is smooth, velvety, tense. There is a definite tache with a white border, and a slight Sergent's line is present in the right upper quadrant of the abdomen, but nowhere else. There is one small pigmented spot at the left side of the chest anteriorly, a few finer spots over the back of the chest and forearms, and a few freckles on the forehead.

The hair distribution shows a scalp covered by dark brown, silky hair, with a posterior straight frontal border and an anterior vertical temporal border. There is a notable absence of hair all over the body. There is a moderate growth of axillary hair. There are a few fine hairs on the back of the forearms and on the legs. There is very scant pubic hair.

The skull is of the brachycephalic type, broad posteriorly, with a prominent occiput. The forehead is receding, but there are very prominent and thickened supra-orbital ridges, more marked on the right side.

The face is broad, with prominent cheek bones. The glabella is broad. The nose is broad. The ears are large, with broad, attached lobules. The eyes are brown, with a slight Mongolian slant. The palpebral fissures are wide. Graefe, Stellwag, Moebius, Dalrymple, and Kocher signs are all negative. There is no nystagmus. There is no evidence of paralysis of any of

the ocular muscles. There is considerable prognathism of the jaw.

Examination of the teeth, by Dr. S. W. A. Franken, shows no teeth missing. The upper centrals are square and small; the left lateral is protruding; there is slightly increased interdental spacing; the canines are broad and flat, the right lateral is small, the right cuspids are broad and small and the lower set of the teeth (anteriorly) are small and broad. The gums are in excellent condition. The color is S. S. White No. 35. All the teeth are short with flat surfaces in the upper set. The dental arch is narrow, palatal arch is high.

The tonsils are small and chronically inflamed. The neck is short and the thyroid is palpable, but not enlarged. The chest is markedly pigeon breasted with a peculiar shape, narrow from side to side and very broad in its anteroposterior diameter; in appearance it resembles a child's chest. There are dilated veins over the manubrium sterni extending upward to the left side and downward to the lower part of the sternum. The breasts are very rudimentary, childlike, no definite nipples, the mediastinal area of dulness is 4¼ inches. The shoulders are round. The lungs are normal and the heart is normal, but the sounds are muffled.

The abdominal wall is slightly adipose; there is no tenderness, no masses, and no rigidity. The lower border of the stomach is made out about a fingerbreadth above the level of the navel. The liver and spleen are not enlarged and the kidneys are not palpable.

The upper extremities are long, not adipose; the hands are broad, the fingers are unusually long, large, bony and square, of the masculine type. The lower extremities are well developed, thighs are not bowed, and there is a slight knock-knee.

Vaginal examination shows introitus is small, cervix is small, pinpoint os, infantile uterus, which is freely movable, and adnexa not felt.

Examination of the nervous system showed no evidence of organic nervous disease.

Examination of the nose and ears was negative.

The urinary examination was negative.

The Wassermann reaction was negative.

x-Ray examination of the skull shows a very small sella turcica with blunted posterior clinoids and peculiar areas on the inner plate of the frontal bone suggesting the possibility of intracranial pressure. Examination of the sinuses showed slight cloudiness of the frontals.

Eye examination (by Dr. Ernest Krug) shows the right eye has decided engorgement of the veins with a pallor of the retina on the nasal side and a blurred disk margin (beginning papillary edema). In the left eye the veins are also engorged, but the outline of the left disk is clear, with no evidence of edema in the retina around it. The fields show an inclination toward a bitemporal hemianopsia with a decided contraction of the color fields, also a tendency to bitemporal hemianopsia.

Discussion.—This patient complains essentially of a periodic, bitemporal, and supra-orbital headache, associated with periodic attacks of nausea and blurring of vision. She has never menstruated and, although she has been married, she has never become pregnant. Objectively we find evidence of a patient with a peculiar gorilla-like appearance, with unusually prominent bone markings of the face, exceptionally large hands which have become so recently, almost complete absence of secondary sexual characteristics, evidence of an infantile uterus and an eye examination which shows engorged veins in both eyes and unilateral papilledema, and a bitemporal hemianopsia for vision and color. We have definite evidence of pressure on the optic chiasm in the characteristic pituitary headache, associated with objective evidence of pressure as shown by the eye-ground examination. There are comparatively few symptoms referable to the endocrine function of the pituitary gland. These are principally the coarse bony features and the enlargement of the hands. The infantile genitals, as well as the absence of breasts and other secondary sexual characteristics, are probably developmental in origin. These latter symptoms, however, suggest that the pituitary disturbance was probably an old one in which cystic degeneration has probably taken place in the

anterior lobe of the pituitary, producing the stimulation of bony growth and the focal pressure symptoms on the optic chiasm.

Case II.—Pituitary Tumor in a Child.—J. F., a little colored girl of twelve years, was referred to the Endocrine Clinic by Dr. Steinbugler in May, 1922, complaining chiefly of headache, accompanied by epigastric pain and fatigability. The illness began about three months before the first visit with headache, which was constant. It was supra-orbital in character, extending just across the head, occasionally in the temples. It was periodic as regards intensity; at certain times it was better than at others. These symptoms persisted until two months before the first visit, when, in addition to the headache, she developed difficulties in vision. The mother noticed it at first on coming home from school, when she would hold her head to the left side and complained of not being able to see out of the right eye. She was taken to a physician on this account, who examined her and found she was blind in the right eye. She was sent to the Lenox Hill Hospital Eye Clinic, examined by doctors Krug and Steinbugler, who had a roentgenogram taken of the skull and referred her to the Endocrine Clinic.

The headaches are always accompanied by attacks of severe epigastric pain. They occur every morning and they become increased until the evening, when fatigability also develops. Since the onset of her trouble she has become very drowsy, in fact, she is so drowsy that she could sleep for twenty-four hours at a time. She has lost her ambition and gets tired very easily. Her bowels move regularly, and she has no convulsions, but she has developed a buzzing sound in the right ear. She has gained somewhat in weight recently. She was a very bright girl in school, but she has been unable to continue with her studies, which is probably due to her failing vision. She is very fond of music. She has not yet begun to menstruate.

Past History.—She had convulsions until three years of age about once a month. She had measles, pertussis, and mumps. She is the last of 6 children, only 1 of whom is living besides herself. She had a normal birth and developed normally.

Habits.—She has a very poor appetite and no fondness for sweets; she does not drink very much water.

Family History.—Her father is alive and well; he is a short, thin, and nervous man. Her mother is well. She is of broad stature. The patient has an older sister seventeen years old who is well. She had 5 other sisters and brothers, one died at birth, another in infancy. One died of pneumonia and one of appendicitis, and one was a still-birth.

Examination shows the following:

Weight	75 pounds
Height	56 inches
Span	59½ "
Lower extremities	27¼ "
Torso	28¾ "
Head, anteroposterior	7 "
Head, lateral	5½ "
Circumference of head	20 "
Circumference of neck	11¼ "
Circumference of chest	23½ "
Circumference of waist	22 "
Circumference of buttocks	32½ "
Pelvis	9½x6 "
Pulse	86
Blood-pressure	70/50

A young, thin girl, with broad features, medium stature for her age. The skin is dry with a rather prominent goose-skin appearance, mulatto color. There is an occasional dark pigmented spot above the right clavicle, the generalized pigmentation is darker over the abdomen and back. The skin is moderately tense, there is a definite tache, but no Sergent's line and no rash. There are a number of leukodermic spots on the right side of the abdomen and on the right side of the sternum.

Hair distribution: The scalp is covered by long, dark, kinky hair with an anterior frontal and anterior temporal border. There are a few long, downy hairs on the forearms. The pubic hair is present, with feminine border. There is a notable absence of hair on the body and lower extremities.

The skull is brachycephalic, broad posteriorly. The supra-

orbital ridges are flat. The ears are very small and round. The glabella is wide, the nose is straight and broad.

The eyes are dark brown in color, rather prominent, with drooping lids and narrow palpebral fissures. Graefe, Stellwag, Moebius, Dalrymple, and Kocher signs are all negative. The pupils of the eyes are round, equal, wide, and react rapidly to light and accommodation. There is no nystagmus.

The teeth are pigmented, with evidence of decay at the roots of many of the teeth in the upper set and at the edges in the lower set. There is a slight notch of the Hutchinson type in the left upper front incisors. The entire upper set points downward and inward. There is no increased spacing. The upper frontals are long and flat. The canines are broad, slightly pointed, and not unusually long. The upper laterals point inward; they are very short, especially the left one. The right lower molars are not completely erupted. On the left side they point inwardly. The palatal arch is moderately high and flat; the dental arch is narrow.

The tonsils are submerged and flat. The neck is of medium size, the thyroid is palpable, but not enlarged. The chest is long and moderately broad, the costal angle is acute. The breasts are moderately developed for the age, nipples are not enlarged. The mediastinal area of dulness is 6 cm. Lungs and heart are normal. The abdomen is not distended, there is no tenderness and no rigidity; liver and spleen are not enlarged, kidneys not palpable. The upper extremities are thin, hands are medium width, fingers long and square. The lower extremities are well developed and there is marked adiposity of the buttocks.

The general configuration is of the feminine type, with lumbar lordosis.

Examination of the nervous system was negative.

The Wassermann reaction was negative.

x-Ray examination of the skull shows normal sinuses, some irregularities on the inner plate of the frontal bone, the sella turcica is quite large, with almost complete destruction of the posterior clinoids, suggesting pressure within the sella.

Examination of the eyes by Dr. Steinbugler shows the vision

in the left eye $\frac{20}{60}$. The right eye is completely blind. Motility of the eyes is normal. There is choked disk of + 4 D. in the right eye. The left eye had beginning optic neuritis and temporal contraction almost to the point of fixation.

Discussion.—This patient began to suffer suddenly with a characteristic pituitary headache, accompanied by attacks of pain in the stomach, nausea without vomiting, and drowsiness. This was followed by progressive loss in vision. We have evidence, objectively, of intrasellar pressure, indicated by the headache and the attacks of nausea and pain, and by choked disk of the right eye. There are, however, few signs suggestive of disturbance in the endocrine function of the pituitary. There is a slight drowsiness and a slight increase in weight. The patient, however, is apparently of the type that we might call the pituitary. She has not menstruated yet, so that we have no evidence of genital disturbance. The Wassermann reaction was negative and she did not respond to intensive antisyphilitic treatment.

II. FUNCTIONAL PITUITARY SYNDROME AND ITS DIFFERENTIAL DIAGNOSIS FROM COMMON ABDOMINAL DISEASES

The diagnosis of the underlying pathology or the disturbed physiology in atypical syndromes in the abdomen is one of the most difficult problems in abdominal diagnosis. The frequency with which we encounter patients suffering with syndromes referable to the gastro-intestinal tract, the bile-ducts, the gall-bladder, and the urinary tract, who still complain of the same symptoms after their abdomens have been decorated with a mass of scars, indicates that the common pathology of these organs does not explain many of the atypical abdominal syndromes, and, indeed, often of the typical syndromes. The difficulty in diagnosing abdominal lesions is well illustrated in the diagnosis of gastric or duodenal ulcer. The presence or absence of ulcer in the stomach or duodenum often remains in doubt even after the most thorough diagnostic procedures have been carried out and the patient has been carefully observed for a long time. Indeed, the diagnosis is still in doubt after the ex-

amination of the stomach and duodenum by the surgeon when he opens the abdomen.

Consequently, it is always timely to call attention to all the possible lesions that may produce abdominal symptoms. A careful study of the patient from every possible angle will frequently enable us to isolate from the atypical abdominal syndromes various disease processes in which the primary lesion or primary disturbance in physiology may be elsewhere than in the abdomen. Moreover, it will permit us to consider other disease processes as probable explanations of some of the typical which they may simulate. We may thus frequently prevent patients from undergoing unnecessary operations which expose a negative or doubtful pathology, and the results of which may be ineffective in modifying the patient's symptoms.

I wish to present a number of cases this afternoon that exhibit dominant abdominal symptoms, which, on clinical grounds, can be proved to be due to disturbance of the pituitary gland. Similar syndromes can and do occur with pituitary tumors, and the close similarity of these syndromes to pituitary tumors, in association with other evidence, is one of the strongest points suggesting the pituitary origin of these conditions.

We have ample evidence that pituitary changes occur without the presence of a tumor, because of the occurrence of headaches exactly similar to those in pituitary tumor before, during, and after menstruation in many patients. Furthermore, there are frequently temporary changes in the visual field occurring at those times, and these changes are frequently associated with abdominal symptoms. Some of the patients that I shall present have been operated upon repeatedly (after the most careful diagnostic study) for all the common surgical abdominal lesions without finding any real pathology, and without relief. Others have been treated for a gastric ulcer or a functional gastric neurosis without much benefit.

In considering, then, the possible lesions or physiologic disturbances that can account for abdominal symptoms, we must consider, especially in the atypical syndromes, the clinical

syndrome that we might term a functional pituitary syndrome. When a most thorough examination of the body and the use of all our present laboratory procedures fail to establish evidence of any of the usual definite abdominal lesions, or when the symptoms of a gastric ulcer, chronic cholecystitis, or symptoms referable to the urinary tract are atypical, the functional pituitary syndrome should be considered as a possible explanation of the symptoms.

The symptoms of this condition are characterized by the occurrence of spasmodic, cramp-like pains in the abdomen. These pains are characterized by not always being localized to the same region of the abdomen. At times they may occur in the epigastrium, the right upper quadrant, the right lower quadrant, the left upper quadrant, or the left lower quadrant of the abdomen. Occasionally, however, repeated attacks may occur in which the cramp-like pains are localized to the same region. A very common location for these pains is the left lower quadrant of the abdomen, simulating an attack of left-sided appendicitis. The attacks are usually accompanied by vomiting or by nausea. In mild cases the attack is merely a periodic, sudden attack of bloating. Many of these attacks simulate an attack of appendicitis or an attack of gall-bladder colic or renal colic. These attacks are *always preceded* by a characteristic supra-orbital and bitemporal headache, which is frequently associated with blurring of vision and dizziness. The attacks are especially common in relation to menstruation. They may occur just before or after menstruation, and they are frequently relieved by menstruation. In rare instances they may occur during menstruation. It is exceedingly common to obtain a history of complete freedom from attacks during pregnancy. The attacks are associated with temperature. A study of these patients from the constitutional standpoint indicates that these attacks are especially common in patients showing evidence of a frank or mild degree of pituitary disturbance either of the Frölich type, the Lorrain-Levy type, or those showing mild degrees of acromegaly. They may also occur in excessively thin women or thin men, showing evidence of eunuchoid character-

istics, as described by Tandler and Gross. The explanation for these attacks is the occurrence of a physiologic or pathologic hypertrophy of the pituitary gland, giving rise to symptoms of increased intrasellar pressure consisting of a characteristic headache, blurring of vision, slight contractions of the visual field, associated with abdominal cramps.

The table on page 702 will indicate the points in differential diagnosis of the functional pituitary syndrome from the common abdominal lesions.

Treatment.—Since the cause of the symptoms in the cases where there is no pituitary tumor is the increased intrasellar pressure, which may be physiologic or pathologic, therapy consists in supplying the body with pituitary extract. The basis for this is that the probable cause of the increased pressure is a physiologic hypertrophy of the pituitary in an effort to supply the necessary hormones. By administering pituitary extract we check the need for hypertrophy, thus relieving the increased pressure. Practically the majority of the patients respond well to such a form of therapy.

Since we are unable to determine the quantitative degree of pituitary need it is impossible to determine the dosage. Some patients respond well to very large doses of pituitary extract and others to very small ones. It is my custom to begin with a definite dose, such as 0.06 gm., and increase the dose if no results are obtained, or diminish the dosage if the headache is intensified or if abdominal cramps are increased or developed. The results of such therapy, for reasons which I cannot explain, seem to be more effective in females than in males. In some of the cases the primary headache which initiates the attack is relieved almost entirely, but the abdominal cramps may be only diminished or not relieved at all. In these instances the use of antispasmodics in large doses (such as atropin or benzyl benzoate) is frequently beneficial in conjunction with pituitary extract. The elimination of proteins from the diet is also distinctly useful, as the work of Dragstedt has recently shown that intestinal putrefaction tends to increase the incidence of spasms. In the eunuchoid types of females, corpus luteum, given by injections

Differential Diagnosis of Pituitary Syndrome

		Pituitary syndrome.	Chronic appendicitis.	Biliary colic.	Renal colic.	Gastric ulcer or duodenal ulcer.	Functional neurosis.
Symptoms.	Pain.	Periodic, cramp-like, in unusual areas, variable as to location; may occur in areas of other lesions.	Right lower quadrant of abdomen.	In right upper quadrant of abdomen, radiating to the back or shoulders; periodic, but always in the same location.	In right or left lower quadrant of abdomen, radiating to the groin or back.	Epigastric or right hypochondriac pain occurring a half hour to two hours after meals.	Epigastric or right hypochondriac.
	Tenderness.	Slight.	Over McBurney's point or external to that.	Over the gall-bladder.	Over the kidney or ureter or in the lumbar region.	Present in epigastrium or right upper quadrant of abdomen.	Present, but not definitely localized.
	Rigidity.	Evidence of localized spasms, but no rigidity.	In right lower quadrant in acute attack.	None, except in acute cholecystitis.	May be present in acute attack.	May be present.	None.
	Vomiting.	Periodic; may be only nausea or attack of bloating. Vomiting may be projectile.	Present.	Present.	May be present.	May occur.	May occur.
	Temperature.	Absent.	Present.	Present in acute cholecystitis.	Present in acute exacerbation.	Absent.	Absent.
	Jaundice.	Absent.	Absent.	May be present.	Absent.	Absent.	Absent.
	Headache.	Supra-orbital, bitemporal, and in relation to menstruation. Precedes the attack.	No characteristic type and follows the attack.	Not specially localized.	Following the attack, but is not specially localized.	Absent.	Absent or not localized. Does not precede attack.
	Gastric analysis.	Normal.	Normal.	Negative.	Normal.	Hyperacidity and blood.	Hyperacidity; no blood.
	Urinary analysis.	Normal.	Normal.	Presence of bile.	May show blood, pus, and crystals.	Normal.	Normal.
	x-Ray examination.	Small, large, or eroded sella turcica; evidence of functional spasm in gastro-intestinal tract which disappears after atropin.	Evidence of adhesions of the appendix.	May show evidence of gall-stones.	May show stones, and pyelograms may show the lesion.	Evidence of defect in pylorus or duodenum.	Evidence of spasm; relieved by atropin.
	Blood examination.	Normal.	Leukocytosis and polynucleosis.	Leukocytosis in acute attack.	In acute pyelitis or pyelonephritis may show leukocytosis. Cystoscopic examination may show evidence of lesion.	May be anemia.	Normal.
	Icteric index.	Normal.	Normal.	Increased.	Negative.	Normal.	Normal.
	Lyon's test.	Normal.	Normal.	Positive.	Normal.	Normal.	Normal.
	Type of patient.	Frölich, acromegalic, Lorrain-Levi, or eunuchoid.	Variable.	Obese or plethoric.	Variable.	Neurotic or hairy.	Neurotic.

or by mouth in large doses will frequently relieve the attacks, either alone or combined with antispasmodics.

Case III.—Pituitary Syndrome Simulating Chronic Cholecystitis and Chronic Appendicitis.—G. E., a young married woman of thirty-four, came under observation in February, 1921, complaining chiefly of cramp-like pains in the left lower quadrant of the abdomen, which were periodic and preceded by supra-orbital and bitemporal headache. She was perfectly well until about eight years previously, when she was pregnant. At that time it was discovered that she had a fibroid uterus. She was operated upon in the fifth month of pregnancy, which was characterized by persistent vomiting, and the fibroid removed. Pregnancy continued and a normal child was born. Following that pregnancy she was well until two years later, when she again became pregnant, and the child was removed in the sixth week of pregnancy for persistent vomiting. For years she has had gas-pains with belching attacks, preceded by supra-orbital and bitemporal headaches. For the last two and a half years these attacks have markedly increased in frequency. They occur almost daily at about 4 or 5 o'clock in the afternoon. The attack begins with a supra-orbital or temporal headache, and is followed by gas-pains and cramps in the left lower quadrant of the abdomen. It is frequently relieved by a bowel movement, but the stool passes in very small quantities.

About a year before her first visit, after a very careful examination, a diagnosis of appendicitis was made and the appendix removed. A marked visceroptosis was found. The appendix, however, was not very much diseased. The attacks persisted after the operation and a very complete *x*-ray examination about a year later demonstrated the visceroptosis and evidence of chronic gall-bladder disease. At operation the gall-bladder was found to be fairly normal, but a gastroptosis was found, which was plicated. For a few weeks after the operation, while she was in bed, she felt better, but the attacks soon recurred, and this is now her chief complaint for which she seeks relief.

Past History.—She had measles, chickenpox, and pneumonia in childhood.

Menstrual History.—Began to menstruate at fourteen, was never regular before marriage, but was always a week overdue. It usually lasts three or four days and is very scanty. She has considerable pain and soreness in both breasts for a week or ten days before menstruation. After marriage menstruation was more regular. She now menstruates every three to three and a half weeks, and it is of the same duration as previously. She has one child.

Habits.—She drinks a lot of milk.

Family History.—The father is alive and well; he is tall and stout. The mother is also tall and stout. The patient has 2 brothers and 2 sisters. The patient is the oldest. The youngest brother has kidney trouble and the youngest sister had a fibroid tumor, appendix, and ovaries removed.

Examination shows the following:

Weight	134½ pounds
Height	61½ inches
Span	58½ "
Lower extremities	30½ "
Torso	31 "
Circumference of head	23 "
Circumference of chest	33½ "
Circumference of waist	28 "
Pelvis	11x6½ "
Pulse	90
Blood-pressure	120/80

A rather broad-statured, nervous young woman. There is no rash on the skin. There is a definite tache, but no Sergent's line. There are a number of freckles on back of both forearms.

Hair distribution: The scalp is covered by dark brown, dry, fine hair with an anterior frontal and an anterior temporal border. There is a slight growth of hair on both forearms and a moderate growth on both legs. Pubic hair has a feminine border; axillary hair is extensive.

The skull is brachycephalic. The forehead is prominent and the supra-orbital ridges are prominent. The nose is broad.

The ears are of medium size, round helix, and attached lobules. The teeth are white in color, in good condition, slight overlapping, especially in the lower set. The palatal arch is of medium height and the dental arch is wide. The throat is congested, tonsils submerged. The neck is short and broad, the thyroid is not enlarged, but is palpable. The chest is broad, with a wide costal angle, the mediastinal area of dulness is 6 cm. The breasts are of moderate size and pendulous. The lungs and heart are normal. There is considerable tenderness in the left lower quadrant of the abdomen. In the right lower quadrant of the abdomen there is a scar about 8 inches long and a similar median one of the same size. There is slight tenderness on pressure in the epigastrium. The lower border of the stomach is present 3 fingerbreadths below the level of the navel. The liver and spleen are not enlarged. The kidneys are not palpable. The upper extremities are thin. The lower extremities are well developed. The general configuration is of broad stature, with epigastric, lower abdominal, and trochanteric adiposity.

Urine examination is negative. Analysis of the gastric contents shows free HCl 20, total acidity 50. Otherwise negative. *x*-Ray report of the gastro-intestinal tract shows evidence of visceroptosis. Examination of the visual field shows no change.

Discussion.—This patient suffered with attacks of cramp-like pains in the lower left quadrant of the abdomen, preceded by characteristic supra-orbital and bitemporal headache. In spite of the fact that her abdomen was opened three times no real pathology in the gall-bladder or appendix or in the urinary tract was found, and the symptoms persisted after several operative procedures. Complete examination failed to demonstrate any definite lesion in the abdomen. The occurrence of the attacks of abdominal pain after a characteristic supra-orbital and bitemporal headache suggested strongly that this patient was suffering from a functional pituitary syndrome. Objectively she showed a mild degree of the anatomic make-up of the Frölich type. She was placed on pituitary therapy and responded well.

Case IV.—Pituitary Syndrome Operated for Chronic Appendicitis and Chronic Cholecystitis.—R. Z. Came under observation in September, 1922, complaining chiefly of periodic headache, vomiting, and upset stomach.

Present History.—The illness began five years ago with headache accompanied by belching, fulness in the throat, and frequently accompanied with vomiting. The attacks always begin with headache and are followed by bloating and vomiting, and they frequently occur after meals. She was treated for this condition for about a year and felt somewhat better. The headaches usually begin at the top of the head and extend to both temporal regions and to the supra-orbital regions and occasionally to the occipital regions. She had attacks of this kind for periods of about six or seven months and then would feel better for awhile. The attacks bear no relation to meals as a rule, and no relation to the kind of food she eats. She has had her tonsils removed for this condition without any benefit. About two months ago the attacks increased both in frequency and in severity. Since then they have been occurring almost every day. They always begin with the characteristic headache in the supra-orbital temporal region and the glabella extending into the eyes, and are followed by severe vomiting. With some of the attacks she gets severe, cramp-like pains in the abdomen, which are sometimes confined to the upper part of the abdomen, at other times to the left lower quadrant, and at times all over the abdomen. She frequently becomes very dizzy with the headaches and she feels very tired. Occasionally the attacks can be relieved by lying down. She has never vomited blood. There has been no change in weight. She perspires excessively. Her bowels have been constipated. The attacks are frequently worse just before menstruation.

Past History.—She has had measles in childhood and has always been subject to grip and tonsillitis.

Menstrual History.—Menstruation began at thirteen and a half years and was always irregular. She menstruates every four or five weeks. The last menstruation was six weeks ago. When she does menstruate it lasts three days if the bleeding is

profuse, or four or five days if it is scant. She feels very weak at her menstrual time. She has the intense supra-orbital headaches and vomiting associated with weakness just before menstruation.

Habits.—She is fond of meat and vegetables, but is not unusually fond of carbohydrates. She drinks 4 or 5 glasses of very weak tea a day. No coffee.

Family History.—Her father is alive and well, fifty-eight years of age, suffers from asthma. He is quite tall and broad. Her mother is alive, about the same age as the father, rather short and stout. She suffers from neuritis and kidney trouble and arteriosclerosis. The patient resembles her father in physique. She has 4 brothers and 2 sisters. The younger brother has epilepsy. All but the youngest are married and have one or two children, and they are all well.

Examination shows the following:

Weight	156 pounds
Height	66¼ inches
Lower extremities	32¾ "
Torso	33½ "
Circumference of the head	21½ "
Circumference of neck	14½ "
Width of shoulders	17½ "
Circumference of bust	36½ "
Circumference of waist	32¾ "
Circumference of buttocks	40 "
Circumference of pelvis	11½x7½ "
Pulse	106
Blood-pressure	100/70.

The patient is a rather tall, broad young woman, whose skin is smooth, soft, velvety, slightly oily, with a definite tache, but no Sergent's line.

Pigmentation: The arms, shoulders, back, and neck are all sunburned, outlining the shoulders of a bathing suit. There are a number of fine pigmented spots on the right arm and a number on the left arm. There are several small pigmented spots on both forearms as well as on the shoulders and neck. There are a few fine acne spots on the back with a small pigmented mole on the outer part of the abdomen on a level with the navel.

Hair distribution: The scalp is covered with coarse, oily, light brown hair with a convex anterior frontal border and a vertical anterior temporal border. The eyebrows are rather thick, arched, extending to the glabella. There is a moderate growth of hair on the upper lip and under the chin. There is some growth of hair around the nipples, extensive axillary hair, with a rather thick growth of hair on the forearms, back of the hands, and fingers. The pubic hair is extensive, with a pyramidal border extending up to the navel. There is a rather thick growth of hair on both legs.

The skull is brachycephalic, broad superiorally, with a straight, convex forehead, with unusually prominent supra-orbital ridges. The ears are small, rather straight helix, and a small, unattached lobule. The face is broad. There is slight prognathism, with prominent cheek bones. The eyes are hazel color and there is a bright expression. The pupils are of medium size, round, equal, they react to light and accommodation. The palpebral fissures are of medium width. Graefe, Stellwag, Moebius, Dalrymple, and Kocher signs are all negative.

The teeth are pearly white in color. There is no increased spacing and no crowding. There is no evidence of decay. The upper frontals are rather broad. The upper laterals are well developed. The upper canines are well developed and pointed. The palatal arch is wide and the dental arch is high. The tonsils are absent (removed); the uvula is absent (removed). The neck is rather short and broad. The thyroid is definitely palpable and slightly enlarged. The supraclavicular areas are rather full, the borders are broad and straight. The chest is long, and costal angle is a right angle. The ensiform is palpable. The breasts are of moderate size, the right is somewhat larger than the left. The nipples are slightly protruding. There is a slight pigmented areola about 1 inch in diameter. The mediastinal area of dulness is 8 c.c. The lungs and heart are normal. The abdomen is not distended. There is distinct tenderness on pressure in the left lower quadrant of the abdomen and slight tenderness in the right lower quadrant, as well as in the epigastrium. The lower border of the stomach is a

fingerbreadth above the navel. The liver and spleen are not enlarged. The kidneys are not palpable.

Upper extremities: The upper extremities are well developed. The hands are broad, the fingers are pointed; there is no tremor. The hands are of the infantile type.

Lower extremities: The lower extremities are well developed, large, and slightly obese.

Adiposity: There is slight adiposity near the axillæ, marked trochanteric and iliac adiposity, with marked gastric and lower abdominal adiposity.

General configuration: The patient is a broad-statured young woman with broad hips and large buttocks.

Laboratory Examinations.—The urine examination is negative. Examination of the gastric contents showed a free HCl 30 per cent.; total acidity 50 per cent. The Wassermann reaction was negative. The basal metabolism was within normal limits. Complete roentgenographic examination of the gastro-intestinal tract showed no evidence of any lesion in the stomach or intestines, only an orthotonic stomach with very active peristalsis. A roentgenogram of the skull showed a very large sella turcica.

Examination of eye-grounds showed no evidence of an optic neuritis or any evidence of pressure, but the perimetric reading showed a slight contraction of the temporal side of both fields.

Discussion.—This patient complained for six years of periodic attacks of supra-orbital and temporal headache associated with vomiting and abdominal cramps in different parts of the abdomen. A very complete examination showed no evidence of any lesion in the gastro-intestinal tract and no lesion in any of the other viscera that were amenable to our present methods of examination. The condition had not responded to treatment throughout the duration of the illness. The occurrence of the characteristic headache associated with abdominal cramps and vomiting, as well as a slight contraction of the temporal sides of both visual fields, indicates that this patient is suffering from symptoms of intrasellar pressure. The prolonged duration of the illness and the severity of the symptoms suggested that there might be a pituitary tumor, but since there were no focal symp-

toms, such as a papilledema, engorged retinal fields, or optic neuritis, it seems likely that such a lesion is not present. The very large sella turcica corroborates the probability of a pituitary origin for the symptoms, but since there is no erosion and no focal eye symptoms a tumor can be eliminated. Examination of the constitutional make-up of the patient indicates that she has the excessive bony growth characteristic of pituitary manifestations, as well as the characteristic adiposity found in the Frölich syndrome. She also has had a relative amenorrhea since the onset of the illness. Consequently, a diagnosis of a functional pituitary syndrome was made and the patient was put on small doses of pituitary. She responded to treatment within three weeks after her first visit and has been free from symptoms at the present writing. She has had no headaches and no attacks of vomiting.

Case V. Pituitary Syndrome with Mild Abdominal Symptoms.—H. M., unmarried, a stenographer, twenty-four years of age, came under observation in October, 1922, complaining chiefly of headaches associated with attacks of nausea.

Present History.—The illness began six years ago when she began to suffer with headache. At that time the headaches were periodic. She would get up every morning with a headache. The headache usually began on the top of the head and extended to the temporal and supra-orbital regions, and they are always associated with a feeling of intense fatigue and intense nausea. For the last year or two the headaches and attacks of nausea have increased in severity so that the condition is almost practically constant, and occasionally she has an attack of vomiting with it. She does not know what initiates the attack. Occasionally she is able to relieve the headache by a dose of any coal-tar product. Since the onset of the illness her weight has remained the same.

Two years ago she was told that a change of climate would benefit her condition, and she went to Colorado, where she remained for about a year, without any benefit. She perspires excessively and frequently has abdominal cramps in association

with the headache, which are not especially localized to any part of the abdomen. Frequently the attacks consist of the headache and bloating without any nausea. Her bowels move regularly. She is not especially nervous. She has no abnormal fears and is not easily excited. She has had considerable treatment for the condition without relief. She has had a deviated septum removed for the condition without any benefit. Her eyes have been examined, and glasses were prescribed for her headaches without any benefit.

Past History.—She has had whooping-cough and measles in childhood.

Menstrual History.—She began to menstruate at thirteen. She is always regular and the menstruation lasts five days. There is no change in the attacks or in the headaches at the time of menstruation.

Habits.—She has a good appetite and is fond of all kinds of food. She is moderately fond of sweets. She drinks about 1000 c.c. of water a day and passes a moderate amount of urine. She is very fond of music and music soothes the headaches.

Family History.—The mother, who was rather stout, died ten years ago at the age of thirty of kidney trouble. Her father is alive and well, tall, and broad shouldered. The patient is an only child and resembles her father. There is no history of similar headaches in any member of her family, most of whom are perfectly well.

Examination shows the following:

Weight	130 pounds
Height	64 inches
Span	63 "
Lower extremities	31½ "
Torso	32½ "
Circumference of head	22 "
Circumference of neck	12¾ "
Width of shoulders	16 "
Circumference of chest	31 "
Circumference of waist	25½ "
Circumference of buttocks	38 "
Pelvis	11x8 "
Pulse	104
Blood-pressure	125/75

The patient is a young girl of medium stature, especially broad features of the face, but a rather narrow body. Her skin is smooth, oily, tense, with a few acne spots on the chest. There is a definite tache. No Sergent's line.

Pigmentation: There are a few pigmented spots over the right shoulder, several over the back of the neck, the forearms, and the arms.

Hair distribution: The scalp is covered by fine silky, oily, dark brown hair, with an anterior frontal and an anterior vertical temporal border. There is a very fine down on the upper lip. There is a moderate growth of axillary hair and there are sparse but long hairs on the back and forearms. The pubic hair is extensive, with a convex border. There are rather sparse long hairs on both legs. The skull is brachycephalic, with prominent forehead and very prominent supra-orbital regions. The face is broad and square, with prominent cheek bones. The ears are long, with a convex helix and unattached lobules. The nose is Roman with a broad tip and there is an evidence of an old fracture of one of the nasal bones. Examination of the nares shows no evidence of any pathology. The eyes are blue in color. The palpebral fissures are wide, the pupils are round, wide, equal, and they react to light and accommodation. There is no nystagmus. Graefe, Stellwag, Moebius, Dalrymple, and Kocher signs are all negative.

There is definite prognathism of the lower jaw, especially marked laterally. The teeth: The color is S. S. White No. 35. There is slight crowding in the upper set; well developed broad upper laterals, broad upper frontals, the canines are long and pointed. In the lower set the canines are unusually large, pointed, twisted, with a stroma between the lower canines and the lower laterals. The palatal arch is wide and the dental arch is narrow. The tonsils are absent (removed). The neck is rather short and narrow. There is slight enlargement of the thyroid, but within normal limits. The chest is long and narrow, the costal angle is acute, the breasts are of moderate size, there are prominent nipples with a moderate areola. The mediastinal area of dulness is 8 cm. The percussion note of the chest is rather hyperresonant,

but is otherwise normal. The heart is normal. The abdomen is slightly distended, especially the lower half. The abdominal wall is voluntarily rigid and there is tenderness on pressure in the left lower quadrant of the abdomen. The lower border of the stomach is on a level with the navel. The liver and spleen are not enlarged. The kidneys are not palpable. The upper extremities are thin, the hands are cold and moist, the fingers are long and square. The lower extremities are well developed.

Adiposity: There is slight epigastric, lower abdominal, and moderate trochanteric adiposity.

General configuration: The patient is short, with a narrow waist and large pelvis.

Laboratory Examination.—Urine analysis was normal. Examination of the gastric contents show free HCl 32; total acidity 48. The basal metabolism was within normal limits. The Wassermann reaction was negative.

Roentgenographic examination of the gastro-intestinal tract showed no evidence of any lesion. Roentgenogram of the sella turcica and sinuses showed a normal sella turcica and no evidence of pathology in the sinuses.

Examination of the eye-grounds was negative and a perimetric reading of the visual field showed a slight contraction of the temporal side of the visual field.

Discussion.—This patient complained chiefly of a syndrome consisting principally in supra-orbital, bitemporal headaches associated with intense headache, attacks of nausea and bloating, but rarely vomiting. The examination of the gastro-intestinal tract showed no evidence of any pathology. Nor could a complete examination reveal any evidence of any organic disease. The syndrome of supra-orbital bitemporal headache associated with attacks of abdominal cramps and nausea are evidence of intrasellar pressure. The increase in severity of the symptoms within the last six months suggested that there might be a tumor within the sella turcica, but a roentgenogram of the sella turcica showed no evidence of erosion nor did an eye examination show evidence of a tumor. Consequently, we were

dealing with a case of a functional pituitary syndrome. The patient was put upon pituitary therapy with a diet in which the proteins were limited, and the symptoms diminished within two weeks after the beginning of treatment, and she is still under observation.

Case VI. Pituitary Syndrome with Marked Abdominal Symptoms in a Growing Boy.—J. G., a young boy of ten and a half years, came under observation in January, 1922, complaining of attacks of abdominal pain preceded by headache and nausea.

Present History.—The patient was well until June, 1921, when he had an attack of intense cramp-like pain in the *right* side of the abdomen. This attack began with bitemporal and supra-orbital headache, was followed by nausea and the cramp-like pains. He had no temperature. The attack lasted a day and he was well again. Two months ago he had another attack. This time the attack began with supra-orbital and bitemporal headache, was followed by nausea, dizziness, and cramp-like pains in the *left* upper quadrant of the abdomen. Since then he has had similar attacks almost every week and at times twice a week. The pain is usually cramp-like and is not always localized to the same region of the abdomen. It always begins with a headache and dizziness, followed by vomiting. The attack lasts a few hours and after the attack the boy is quite well again. Frequently on lying down the attack subsides in a few hours. His mother has used a hot-water bag without any relief. For the last few months, in addition to the attacks, he gets up every morning feeling dull, drowsy, and stupid, and frequently complains of supra-orbital headache and dizziness without getting the attacks. He is very constipated. Since the onset of the illness he has lost in weight, although previously to this he had gained considerable weight. He is thirsty practically all the time. He drinks 3000 c.c. of water a day and passes an almost similar quantity of urine. He goes to school, is a bright boy, is fond of arithmetic, and gets practically 100 per cent. in all his studies. At home he is quiet and well behaved, preferring to sit at home and study and not caring to play much with other children. In

fact, his quiet habits are expressed by his mother in the words that "he should have been a girl instead of a boy."

Past History.—The patient was a normal child, normal delivery, had measles at the age of two, and at the age of four he had his tonsils and adenoids removed because of an otitis media. He had a discharge from his ears for awhile which responded to treatment. He has had mumps. Following the removal of his tonsils and adenoids he became much stouter. His first teeth came at the age of six months; he could raise his head at the age of eight months, began to talk at the age of a year, and began to walk at the age of sixteen months.

Habits.—He is very fond of candy and cake, drinks a good deal of milk, and drinks water excessively.

Family History.—The father is thirty-two years of age, short and stout, weighs 190 pounds. He suffers a good deal from swelling around the joints. The mother is twenty-nine years of age, of medium stature, weighing 135 pounds, and is perfectly well. The patient has a sister four and a half years of age who is thin and nervous. His maternal grandfather died of meningitis at forty-two.

The patient's uncles and aunts on his father's side are all short and stout.

Examination shows the following:

Weight	65½ pounds
Height	51½ inches
Span	51 "
Lower extremities	25 "
Torso	26½ "
Circumference of head	19½ "
Anteroposterior	7 "
Lateral posterior	5½ "
Circumference of neck	11 "
Circumference of chest	24¾ "
Circumference of waist	23 "
Circumference of buttocks	27½ "
Pelvis	8x5 "
Pulse	110
Blood-pressure	140/70

The patient is a rather short, well-developed, broad-statured, and broad-featured boy of dark complexion. His skin is dry, smooth, adipose, moderately tense. There is no rash. There is a slight tache, no Sergent's line. Veins over the left side of the chest are moderately dilated, extending upward and downward to the front of the left shoulder and the upper part of the arms.

Pigmentation: There are a few slightly pigmented spots on the manubrium, sternum, and a large pigmented spot to the left of the lower part of the chest. There is a small pigmented spot on the left side of the abdomen and an elongated spot about 1 inch long midway between the navel and pubis.

Hair distribution: The scalp is covered by very fine, beautiful curly and silky black hair, with a marked anterior frontal border and anterior vertical temporal border. The eyebrows are very bushy. There is a slight growth of hair over the glabella, a few downy hairs over the cheeks, and a slight downy moustache. There are a few downy hairs along the cheeks. There is a marked growth of thin hair along the spine extending upward toward the scapula. There is a slight growth of hair on the arms and back of the forearms, and a marked growth of hair on the legs and a very few lanugo-like pubic hairs.

The skull is brachycephalic, the forehead is prominent, straight, with prominent supra-orbital ridges, rather broad, but oval face. The general expression of the face is that of an adult rather than that of a child. The nose is concave, broad, soft at the tip, slightly retroussé.

The examination of the nares was normal. The ears are round, the lobes are present, but attached. Examination of the drum membranes showed no evidence of pathology. The eyes: There is a slight edema around the eyelids. The eyes are brown, the palpebral fissure is of medium width, and the pupils are round, of moderate width, equal, and react to light and accommodation. There is no nystagmus. No exophthalmos. Graefe, Stellwag, Moebius, Dalrymple, and Kocher tests are all negative. The lips are thick. There is no prognathism of the jaw. The teeth are pigmented, especially in the lower set, with slight

infection of one or two of the roots in the lower set. The upper front incisors and upper laterals are broad and short, the canines are short, and there is an increased dental spacing between the upper frontal incisors. The throat is congested. The tonsils are absent (removed). The neck is of medium length, the thyroid is not enlarged. The chest is broad. The costal angle is wide, the ensiform is palpable. There is slight pigmentation around very tiny nipples. The lungs and heart are normal. The abdomen is not distended. There is no tenderness or rigidity. The lower border of the stomach is present at the level of the navel. The liver and spleen are not enlarged. The kidneys are not palpable. The upper extremities are thin. The hands are broad, cold, and moist, the fingers are long and square, and there is no tremor. The lower extremities are rather thin. He is knock-kneed. The legs are thin and the feet are broad with long toes.

Genitals: There is a large inguinal ring on both sides. The right testis is undescended, not felt. It comes down at times, but is much smaller than the left. The left testis is in the scrotum, of normal size, the penis is rather small.

The general configuration is of a boy of short, broad stature, with slight epigastric, and lower abdominal adiposity.

Laboratory Examinations.—The urine examination is normal. The basal metabolism is within normal limits. Examination of the autonomic nervous system showed no evidence of autonomic imbalance. Roentgenogram of the skull showed a normal sella turcica.

Examination of the eye-grounds showed no evidence of pressure and the perimetric reading showed no change in the visual field.

Discussion.—This patient, a growing boy, began to suffer with periodic attacks of supra-orbital and bitemporal headache associated with severe cramps in the abdomen and nausea. One of the attacks resembled an appendicitis attack, but there was no temperature. The attacks have increased in frequency and are associated with excessive thirst and polyuria. A complete examination showed no evidence of any organic disease in the

abdomen and no evidence of any other organic disease. The patient, however, showed measurements indicating pituitary domination in growth, a slightly pituitary type of adiposity, and an increased interdental spacing. We may consider the characteristic headache and attacks of cramp-like pains in the abdomen as evidence of intrasellar pressure, probably due to physiologic hypertrophy of the pituitary incident to growth and development.

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THE PROGRESS OF POTENTIALLY DIABETIC PERSONS IN RELATION TO DIETARY CONTROL

THE object of this paper is to report the progress of a series of cases of supposed latent or potential diabetes. The majority of them had never suffered from the usual diabetic symptoms, but became the objects of study on account of a suspicion of diabetes due to hereditary influences. The glucose tolerance test was used as an index of the impairment of carbohydrate assimilation. The former dependence on urinary analyses alone would have proved misleading in the majority of the cases in the early stages. The use of the blood-sugar determinations permitted more reliable diagnosis of the true condition, and was used as a guide in prophylaxis.

The cases have been observed over a sufficiently long period of time to secure some idea of either gain or loss of tolerance and the connection with fidelity to diet.

Cases I and II showed definite loss of tolerance due to failure to observe simple dietary rules, which were prescribed following the diagnosis of their potentially diabetic condition. Case I was observed over a period of two and a half years, during which time there was steady and gradual loss of carbohydrate assimilation, as shown by the constancy with which hyperglycemia more readily developed as time passed. The first glucose tolerance test (performed June 8, 1921) resulted in only slight elevation of the plasma sugar curve above normal without glycosuria, but the loss of tolerance through continued pancreatic overstrain is shown by the tests performed one year and

two years later, when glycosuria and more marked hyperglycemia occurred. In this case the patient, contrary to advice, allowed himself to become overweight, and indulged himself in large amounts of carbohydrate foods. Case II showed downward progress and loss of tolerance similar to Case I, but the period of observation was much shorter. When first seen the history was suspicious of diabetes, and a glucose tolerance test confirmed the possibility of an existing mild diabetes. Simple reduction of body weight would most probably have served to keep the case well under control, but due to lack of co-operation on the part of the patient and his insistence upon continued indulgence in diets of high caloric value, control of the trouble was lost. Instead of reducing his body weight as advised, he gained 10 pounds during the two months that elapsed between the two observation tests. Glycosuria resulted from the ingestion of 100 gm. of glucose during the second test, whereas it was absent on a similar amount of glucose on the initial test. Severe intoxications or infections did not occur during the observation periods in these 2 cases, so loss of tolerance due to these factors would not be a possibility.

The other cases cited in this communication apparently represent arrested development of diabetic tendencies in potentially diabetic persons by limitation of diet. Cases III and IV are brothers, whose history revealed many diabetic relatives. When first seen (May 4, 1921) they were tested simply on account of the hereditary history. Their diets had always been normal. Glycosuria resulted in both cases during carbohydrate tolerance tests. The amount of glucose excreted was small in each instance, and the kidney thresholds were relatively low. Case III was overweight, with a natural tendency to obesity. So he was advised to reduce his weight sufficiently to prevent obesity, but not sufficiently to prevent actual growth. Adherence to these principles had its good effect, with gain in carbohydrate tolerance, as shown by the improvement in assimilation when the test was repeated a year later. His weight, which was 90 pounds with clothes on May 4, 1921, with a height of 4 feet, 8 inches, was reduced to 86 pounds with clothes

on May 13, 1922, but the height had increased to 4 feet, 9½ inches. Case IV likewise adhered to rigid diet measures. Sugar was not used at any time, but occasionally he took bread. He remained on low nutrition throughout the year, and gained only 4 pounds in weight, although his height increased from 5 feet, 5 inches to 5 feet, 6½ inches. The second glucose tolerance test showed an improvement over the previous one, since the plasma sugar curve did not remain elevated over as long a period of time as the first one, and glycosuria did not occur. Even though considerable improvement was shown in the second tolerance test, the curve was not a strictly normal one. This case, like Case III, may be regarded as still in a potentially diabetic state. Both patients are still following diet precautions and keep their body weights within normal limits.

Case V was that of a young girl of seven, in whom downward progress was arrested by a long period of undernutrition. Gain in tolerance was associated with the undernutrition, which was instituted from January 6 to July 22, 1922. There can be but little doubt that true diabetes mellitus existed, since she gave a history of loss of weight, glycosuria, and acidosis on admission. The presence of sugar in the urine and a high plasma sugar of 275 mg. per 100 c.c. on July 22d also bears out this suspicion. Diet was abandoned on July 22d on account of the parents' belief that diabetes did not exist. The strict period of undernutrition with gain in tolerance enabled her to resume the use of all forms of high class carbohydrate foods without return of glycosuria or a return of diabetic symptoms, but the observation period since the change to such diet is too short to show possible downward progress and loss of tolerance through pancreatic overstrain.

Case VI is also one in which advance of the diabetic condition has been delayed by restriction of diet. Frank diabetic symptoms were not present at the time of the initial discovery of glycosuria, neither have they appeared since. The results of the two tolerance tests taken a year apart are similar, but the second one was taken during the presence of an infection, which may account for the appearance of the very faint trace of sugar.

From the date of the first test (October 12, 1921) to March 1, 1922 the diet was more closely restricted than from the latter date up to November 23, 1922. During the first period she was allowed only low class carbohydrate foods, with bread and cereals only occasionally. There was definite gain in tolerance, as shown by the normal digesting plasma sugar of 118 mg. per 100 c.c. on December 31, 1921, and 136 mg. per 100 c.c. on March 1, 1922. On the latter date a liberal increase in diet was given, including bread and cereal daily. The weight gradually increased to 35½ pounds on March 23d. Slight loss of tolerance due to relaxing the stricter dietary program previously mapped out for her was shown by the increase in plasma sugar to 150 mg. per 100 c.c. on August 2, 1922, and 152 mg. per 100 c.c. on November 22, 1922. The glucose test performed November 23d was hardly a fair test of tolerance, due to existing bronchitis and rhinitis at the time. A repetition of the test a few weeks hence after signs of infection have subsided will be of considerable interest, and will give a truer index of her real power of assimilation. At no time has there been a suspicion of the presence of diabetes in the ordinary sense. She has continued in a good state of nutrition, but free from obesity. If the tolerance test may be used as a criterion of the individual's ability to metabolize carbohydrate, the diabetic element in this particular case may be considered arrested.

Case I.—Male. Hebrew. First seen June 8, 1920 at age of seventeen. Height 5 feet. Weight 122 pounds.

The patient's personal history was negative. His mother died of diabetic coma at the age of thirty-two. A sister, aged nineteen, has diabetes. A maternal aunt of thirty-seven has diabetes of mild degree.

The past history was negative, and on close questioning none of the early symptoms of diabetes could be elicited. With the exception of a tendency to obesity, the physical examination was negative.

On June 8, 1920 a glucose tolerance test was performed at the request of the boy's father, who desired any information

concerning any possible early tendency to diabetes. The interesting findings and investigations in this particular case had their beginning only in groundless suspicion, and not in any fact or symptom indicating the presence of diabetes. The results of the first test showed a diabetic tendency; 100 gm. of glucose by mouth caused a rise in plasma sugar from 118 mg. per 100 c.c. to 207 mg. per 100 c.c. within one hour. At the end of the second hour there was only a slight remission to 162 mg. per 100 c.c., but at the end of the third hour it had fallen to 100 mg. per 100 c.c. Glycosuria did not occur throughout the four-hour period of observation. In accordance with strict standards the curve could not be pronounced normal, but should be classed as "prediabetic" or "potential." The results of the test are shown in Table I. The patient was advised to take precautions to avoid pancreatic overstrain by regulation of diet. Neither at this time nor during the ensuing years that he has been under observation has he taken his condition seriously. The advice given him, namely, restriction of concentrated carbohydrate foods, against overindulgence, restriction of the total diet, and prevention of obesity, bore no weight with him. He has disregarded diet practically the entire time. Gradual loss of food tolerance has been noted in his case.

TABLE I.—CASE I.

Date.	June 8, 1920.			May 25, 1921.			October 13, 1922.		
Hour.	Plasma sugar mgm. per 100 c.c.	Urine vol. c.c.	Urine dextrose per cent.	Plasma sugar mgm. per 100 c.c.	Urine vol. c.c.	Urine dextrose per cent.	Plasma sugar mgm. per 100 c.c.	Urine vol. c.c.	Urine dextrose per cent.
Before glucose	118	150	0	110	118	0	168	220	0
½ hour after	...	...	...	226	...	...	306		
1 " "	207	50	0	242	Unable to void		351	88	0.54
2 hours after	162	205	0	187	46	0.26	341	117	0.98
3 " "	...	270	0	92	45	0	203	110	0.35
4 " "	100	300	0	101	95	0			

From the date of the glucose tolerance test until January 1, 1921 he followed diet fairly well, and conformed to the required regulations the greater part of the time. Several office calls were made. On September 14, 1920 a blood analysis taken during

digestion of a meal showed a normal sugar value of 129 mg. per 100 c.c.; also, on October 22 and November 19, 1920, the tests were 102 and 131 mg. per 100 c.c. respectively during digestion. On December 20th, however, after becoming lax with the diet, distinct hyperglycemia of 164 mg. per 100 c.c. was found. Beginning January 1, 1921 he gave up dietary measures entirely and ate normal quantities and kinds of food. He gained rapidly in weight.

A second glucose tolerance test was performed a year later (May 25, 1921), and it showed definitely that tolerance had been lost, since hyperglycemia of greater degree resulted. The test was performed under identically the same conditions as the previous one, and the same amount and kind of glucose was used. A higher and more prolonged hyperglycemic curve was produced. The blood-sugar rose from 110 mg. per 100 c.c. to 126 mg. per 100 c.c. within a half-hour. By the end of the first hour it increased to 242 mg. per 100 c.c. The patient was unable to void at the end of the first hour period, but glycosuria of 0.26 per cent. was present at the second hour period. The blood-sugar at that time was 187 mg. per 100 c.c. At the end of the third hour the blood-sugar returned to normal. The results are shown in Table I. He was again advised and warned about the necessity of proper dieting, but he made little or no attempt in this direction.

Three office calls were made during the following year. Blood analyses made at these visits were unsatisfactory, all of the determinations showing increasingly higher results. On July 6, 1921 a fasting blood specimen taken before breakfast showed definite hyperglycemia of 148 mg. per 100 c.c. Again, on September 9, 1921, marked hyperglycemia of 290 mg. per 100 c.c. resulted, and on December 23, 1921 he had hyperglycemia of 166 mg. per 100 c.c. Glycosuria was not found on several examinations. He continued to gain in weight, from 126 pounds in July, 1921, to 132 pounds in December, 1921.

A third glucose tolerance test was performed October 13, 1922. His height was 5 feet, 2 inches, with a weight of 135 pounds, with clothes. He had not followed diet. He was

overweight and there were large deposits of fat on the abdomen and chest. Two weeks previously he had a number of furuncles on the face, which healed slowly. During the year which had elapsed since his last tolerance test he had had a number of boils on the face and neck, but they were not of a serious nature and healed readily when carbohydrate was temporarily restricted. He had examined the urine on several occasions during the year, but sugar was not found at any time. The plasma sugar curve was diagnostic of diabetes. The test was performed three hours after the patient had had breakfast. The plasma sugar at that time was found to be 168 mg. per 100 c.c., which in itself would cause one to be suspicious of diabetes. The urine specimen before the glucose tolerance test was negative for sugar; 100 gm. glucose was administered by mouth. Within thirty minutes the plasma sugar had increased to 306 mg. per 100 c.c. One hour later it showed even a higher value of 351 mg. per 100 c.c., and the urine contained 0.54 per cent. sugar. At the end of two hours there was only slight remission in plasma sugar to 341 mg. per 100 c.c. and the urine sugar had increased to 0.98 per cent. By the fourth hour the plasma sugar had decreased to 203 mg. per 100 c.c. and the urine sugar had decreased to 0.35 per cent. The reducing substance was verified as glucose with fermentation test. Results of the test are shown in Table I.

Case II.—Male. Hebrew. Age twenty-nine. Clerk. First seen March 9, 1921. Height 5 feet, 8 inches. Weight 196 pounds.

The family history was negative for diabetes. The past history was practically negative, except that he was a hearty eater and always indulged in an abundance of carbohydrate foods. He had no infections except a slight attack of tonsillitis five months ago.

Six months ago he was examined for life insurance and a trace of sugar was found in the urine. Two subsequent tests were found negative, and he was passed as a first class risk. He afterward followed no particular diet. Four months ago boils developed on the face, and he had a series of carbuncles on the

neck. Sugar was present in the urine at that time. He was advised to avoid starches and sugars, which he did, and glycosuria remained absent until one month ago, when, after abandoning diet, glycosuria returned. Several analyses during the past week showed 1 per cent. sugar, but during this time he was ingesting normal amounts of sugar and starch. His highest weight is the present weight of 196 pounds.

He was first seen March 9, 1921. A blood specimen taken an hour after a meal consisting of meat, vegetables, and a slice of rye bread was found to be 115 mg. per 100 c.c. From the history it was judged that he had a very mild or incipient diabetes, but further laboratory findings were necessary to confirm the diagnosis. On March 17th he reported for another blood analysis. After a heavy carbohydrate meal, consisting of bread, sugar, pastry, meat, and vegetables, a sugar of 136 mg. per 100 c.c. was noted one hour after the meal. The urine was sugar free.

On March 27th a tolerance test was performed, with 100 gm. of glucose by mouth. The results are shown in Table II. The test was performed without breakfast. The plasma sugar at that time was found to be 114 mg. per 100 c.c., and the urine was negative for sugar. One-half hour after the ingestion of glucose the plasma sugar had risen to 166 mg. per 100 c.c., and at the end of the hour period to 192 mg. per 100 c.c. Hyperglycemia declined rapidly to 120 mg. per 100 c.c. at the second hour, and to 93 and 95 mg. per 100 c.c. at the third and fourth hours respectively. Glycosuria did not occur. The figure of 192 mg. per 100 c.c. at the end of the hour period is slightly above normal, but the record did not afford any positive diagnosis of diabetes. The most probable interpretation was that a mild degree of pancreatitis, without physical signs or symptoms, existed, and that the condition was probably acute in character.

To guard against danger of prolonged functional strain he was advised to follow a moderately restricted diet, and especially to restrict high class carbohydrate foods. He was also advised to reduce the body weight at least 5 or 10 pounds.

TABLE II.—CASE II.

Date.	March 26, 1921.		May 24, 1921.	
Hour.	Plasma sugar mg. per 100 c.c.	Urine dextrose per cent.	Plasma sugar mg. per 100 c.c.	Urine dextrose per cent.
Before glucose	114	0	126	0
½ hour after	166	0	206	0
1 " "	192	0	125	0.18
2 hours after	120	0	93	0
3 " "	93	0	80	0
4 " "	95	0	102	0

He was again seen May 24, 1921. He had not conformed to the above advice given him, but, to the contrary, had used sugar moderately and had partaken of normal quantities of food. His body weight had increased to 206 pounds. No urine examinations had been made since his last visit.

On the return visit a second glucose tolerance test was performed in identically the same manner as the first. The results are shown in Table VI. A blood specimen taken before he had had breakfast and before the administration of glucose was found to be 126 mg. per 100 c.c. The urine was negative for sugar. One-half hour after the ingestion of 100 grams of glucose by mouth the plasma sugar had increased to 206 mg. per 100 c.c., but at the end of the one-hour period had decreased to 125 mg. per 100 c.c. Glycosuria to the extent of 0.18 per cent. occurred at the end of the one-hour period. The plasma sugar decreased to 93 and 80 mg. per 100 c.c. at the end of the second and third hours respectively, but glycosuria did not occur.

Case III.—Male. Age nine. Danish. First seen May 24, 1921. Height 4 feet, 8 inches. Weight 90 pounds.

This patient is a brother of Case IV. On account of the family history of diabetes a glucose tolerance test was performed May 24, 1921. The mother died of diabetes at the age of forty. One brother, aged twelve, has diabetes mellitus of mild degree. The father is obese, and showed heavy glycosuria after the ingestion of 100 gm. of glucose.

The past history was negative. He was always strong and

active, but inclined to obesity. He was fond of all foods, but never overindulged in carbohydrate or any other special articles. Physical examination was negative, except that he was overweight, and had a large accumulation of fat over the abdomen and thighs.

On May 24, 1921 he was given 100 gm. of glucose by mouth. The results are shown in Table III. The test was performed at 8 A. M. before he had taken breakfast. A blood specimen before ingestion of glucose was found to be 108 mg. per 100 c.c. and the urine was negative for sugar. At the end of one-half hour hyperglycemia of 209 mg. per 100 c.c. occurred. A few minutes after taking the blood specimen at the end of the half-hour period the test was partially interfered with due to vomiting, but it was completed. At the end of the hour period a blood analysis showed a normal plasma sugar of 94 mg. per 100 c.c., but glycosuria to the extent of 0.086 per cent. occurred. Blood tests at the end of the second and third hour periods revealed plasma sugars of 84 and 130 mg. per 100 c.c. respectively, without glycosuria.

TABLE III.—CASES III AND IV

	Case III.				Case IV.			
Date.	May 4, 1921.		May 13, 1922.		May 4, 1921.		May 13, 1922.	
Hour.	Plasma sugar mgm. per 100 c.c.	Urine dextrose per cent.	Plasma sugar mgm. per 100 c.c.	Urine dextrose per cent.	Plasma sugar mgm. per 100 c.c.	Urine dextrose per cent.	Plasma sugar mgm. per 100 c.c.	Urine dextrose per cent.
Before glucose	108	0	116	0	125	0	118	0
½ hour after	209[1]	..	138	..	189	..	270	
1 " "	94	0.086	180	0	214	0.398	169	0
2 hours after	84	0	150	0	166	0	125	0
3 " "	130	0	107	0	136	0	75	0
4 " "	...	..	...	..	93	0		

[1] Vomited.

On account of his tendency to obesity, the history of diabetes in the family, and the occurrence of glycosuria during the tolerance test a reduced diet was advised. During the year he avoided sugar entirely, but occasionally used bread and potatoes, but

only in small quantities. On the whole, he followed an anti-diabetic diet. He was advised to prevent a rapid increase in body weight, but to take a diet sufficiently liberal to permit normal growth.

He returned for a second glucose tolerance test a year later (May 13, 1922). His height had increased to 4 feet, 9½ inches, but the weight was 84 pounds—6 pounds less than the preceding year. A similar amount of glucose and of the same kind given the preceding year was administered. The test, like the previous one, was performed at 8 A. M. before breakfast was taken. A plasma sugar before ingestion of glucose showed 116 mg. per 100 c.c. and the urine contained no sugar. The sugar at the half-hour period rose to 138 mg. per 100 c.c., and further to 180 mg. per 100 c.c. at the hour period. At the end of the two- and three-hour periods the plasma sugar decreased to 150 and 107 mg. per 100 c.c. respectively. Glycosuria did not occur during the test.

This case, like the following one, most probably represents increased carbohydrate tolerance, due to the restricted diet which was taken during the intervening year.

Case IV.—Male. Age fourteen. Danish. Seen May 24, 1921. Height 5 feet, 5 inches. Weight 105 pounds.

This patient is a brother of Case III. On account of the family history of diabetes a glucose tolerance test was performed May 24, 1921. The mother died of diabetes at the age of forty. One brother, aged twelve, has diabetes mellitus of mild degree. The father is obese, and showed heavy glycosuria after the ingestion of 100 gm. of glucose.

The past history was negative. He had always been thin and undernourished, in spite of the fact that his appetite was normal and he ate liberal quantities of food. The present weight of 105 pounds is the greatest he had ever attained. He had never had polyuria, polyphagia, or polydipsia. The physical examination was negative except that he was undernourished and had a peculiar olive complexion.

The results of the glucose tolerance test after the ingestion

of 100 gm. of glucose by mouth is shown in Table III. The test was performed at 8 A. M. before breakfast had been taken. A fasting blood-sugar of 125 mg. per 100 c.c. was noted previous to the administration of glucose. One-half hour later it had increased to 189 mg. per 100 c.c., and one hour later had increased further to 214 mg. per 100 c.c., and sugar appeared in the urine to the extent of 0.398 per cent. The reducing substance was positive to the fermentation test. At the end of the two-hour period hyperglycemia had decreased to 166 mg. per 100 c.c., and further to 136 mg. per 100 c.c. at the end of the three-hour period. Such response to 100 gm. of glucose by mouth may safely be considered as diagnostic of diabetes. In view of the positive findings he was instructed to restrict the diet.

During the following year he avoided sugar, pastries, and sweets entirely. He was at all times faithful to diet, being encouraged by his father, who knew the danger of diabetes.

In May, 1922, a year after the initial tolerance test, a second one was performed. During the year he had increased in height 5 feet, 6½ inches, while the weight had only increased to 109 pounds. He was strong and athletic. He had had no infections or serious illnesses of any kind during the intervening year. One hundred gm. of glucose were administered at 8 A. M. before he had had breakfast, the test being performed with the same quality of glucose and in a manner identical with the previous one. The results are also shown in Table III. The plasma sugar before administration of glucose was 118 mg. per 100 c.c. At the half-hour it increased rapidly to 270 mg. per 100 c.c., but at the end of the hour period it had fallen to 169 mg. per 100 c.c. The blood-sugar at the end of the second and third hours was found to be 125 and 75 mg. per 100 c.c. respectively. Sugar did not appear in the urine. Apparently he had gained tolerance during the year, due to his adherence to diet and the fact that he avoided a high calorie diet and had not increased in body weight.

Case V.—Female. American. Age seven. First seen January 6, 1922. Height 3 feet, 10 inches. Weight 41 pounds.

Past History.—The patient's family history was negative for diabetes. She was always of small stature, but inclined to be muscular. Her maximum weight was 47 pounds in February, 1921. There had never been a sudden loss of weight. She never had jaundice or epigastric cramp or pain.

In March, 1919 she had diarrhea and vomiting, which continued for a week. She lost 4 pounds in weight and her skin became dry. Polyuria and thirst were not present. The condition was diagnosed as acidosis, but sugar was not present in the urine. Heavy acetonuria was present. The fats in the diet were restricted, and she was given a carbohydrate diet, on which the symptoms disappeared. The doctor advised later that she be given a normal diet, with the exception of sweets. The child grew slowly after the attack of acidosis.

From the time of the first attack in 1919 until three weeks ago the urine was not examined. Then the patient lost appetite and had nausea and vomiting. Her weight decreased 2 pounds. A urine examination revealed heavy sugar and acetone. Daily tests on three following days showed sugar present. The diet was not altered to any extent, and examination two weeks later showed sugar still present. She was put on a restricted diet, and a urine examination later proved negative for sugar. She continued to lose weight, felt drowsy, and complained of fatigue and weakness. The mother noticed that the breath had a sweetish odor. Polyuria and thirst were present.

She was first seen January 6, 1922. A blood analysis taken during digestion of the noon meal contained sugar to the extent of 211 mg. per 100 c.c. The urine was negative for sugar and the acetone reaction was moderate.

She was admitted to the Institute January 6, 1922. The results of her progress in the hospital and subsequent office calls are shown in Table IV. The urine was strongly positive to the nitroprussid test. She was given a diet of 25 grams of protein, 35 grams of carbohydrate, and 20 grams of fat. This was a much lower diet than that to which she had been accustomed. The acetone reactions in the urine continued heavy, and on January 10th she had nausea and vomiting. A blood speci-

men taken before breakfast showed a plasma sugar of 104 mg. per 100 c.c., with a carbon dioxid combining power of 48.1. On January 11th acidosis became intense, with headache, drowsiness, nausea, and vomiting. The nitroprussid test showed a heavy reaction, but the ferric chlorid test was negative. The diet was immediately changed to 50 grams of carbohydrate without protein or fat. Such diet was continued throughout January 11th and 12th. On January 13th the diet was modified so that she received 40 grams of protein, 40 grams of carbohydrate, and 17 grams of fat. The urine remained negative for sugar, but the acetone reaction was heavy. On January 14th, on the same diet, a blood analysis showed a digesting sugar of 131 mg. per 100 c.c., and on January 17th, 153 mg. per 100 c.c. At no time did sugar appear in the urine, but occasionally there was an odor of acetone on the breath, and the nitroprussid reactions continued strongly positive. On January 22d, on a diet of 55 grams of protein, 30 grams of carbohydrate, and 700 calories, a digesting blood-sugar was found of 184 mg. per 100 c.c. She was discharged January 23d, and instructed to continue the 700 calories diet at home. During her stay in the Institute her body weight was reduced from 41 to 37 pounds.

On January 30th she returned for an office call. The plasma sugar was found to be 110 mg. per 100 c.c. during digestion of the noon meal, and the diet was accordingly increased to 55 grams of protein, 30 grams of carbohydrate, and 850 calories. Following are the plasma sugar analyses made upon subsequent office calls, all determinations being made during digestion of the noon meal: February 13th, 111; March 5th, 126; March 28th, 119; April 23d, 134; May 14th, 149; July 1st, 140 mg. per 100 c.c. At each office call the diet was gradually increased in protein, fat, and carbohydrate, until July 1st it had been built up to 70 grams of protein, 60 grams of carbohydrate, and 1400 calories, with regular weekly fast days of 45 grams of protein, 35 grams of carbohydrate, and 900 calories. At no time did sugar appear in the urine. The child's body weight gradually increased to 42 pounds. The symptoms of acidosis did not return at any time.

TABLE IV.—CASE V

Date, 1922.	Diet.				Urine.		Blood.		Body weight, pounds.	
	Protein, gm.	Fat, gm.	C. H., gm.	Total calories.	Qualitative dextrose.	Qualitative nitro-prussid.	Plasma sugar mg. per 100 c.c.	CO_2 vol. per cent.		
January										
6	New York	Office.		...	..	....	211[1]			
9	13	0	13 (2 meals)	...	..	....	....	....	..	Admitted.
10	25	20	25	...	0	Heavy.	104	48.1		
11	..	..	50	...	0	"	....	....	41	
12	..	..	50	...	0	Mod.	....	....	..	
13	40	17	40	...	0	Heavy.	....	....	40	
14	40	7	40	...	0	"	131[1]			
15	40	2	40	...	0	"	....	....	39	
16	40	2	40	...	0	"	....			
17	40	..	40	...	0	"	153[1]	58.1	39	
18	45	43	20	650	0	"				
19	45	43	20	650	0	"	097[1]	....	36	
20	55	62	30	900	0	"				
21	55	62	30	900	0	Mod.	....	....	36	
22	55	40	30	700	..	....	184[1]	60.0		
23	..	..	..	...	..	....	....	....	37	Discharged.
30	55	40	30	700	0	Ft.	110[1]	....	38	Office call.
February 13	55	49	30	850	0	Ft.	111[1]	....	38	"
March 5	55	69	40	1000	0	0	126[1]	....	39	"
28	60	73	50	1100	0	0	119[1]	....	40	"
April 23	65	82	50	1200	0	0	134[1]	....	40	"
May 14	65	82	50	1200	0	0	149[1]	....	40	
July 1	70	97	60	1400	0	0	140[1]	....	42	
22	70	97	60	1400	0	0	135[1]	....	42	
					Mod.	0	275[1]	....	..	One hour after saccharose.

[1] Specimens taken during digestion of meals.

On July 22d a single blood determination taken during digestion of a meal was found to be 135 mg. per 100 c.c. The urine was negative for sugar and acetone. On that date 60 grams of saccharose were administered by mouth. A blood analysis secured one hour later showed the plasma sugar to be 275 mg. per 100 c.c., with moderate glycosuria. She was instructed to continue the 1400-calorie diet.

On August 1, 1922 she changed to another physician, who abandoned treatment and diet in the belief that diabetes did not exist, and she took a general diet with the exception of starch and sugar. Body weight rapidly increased to 47 pounds. By September 15th sugar had not appeared in the urine, and then forced feeding was begun in the attempt to increase body weight, which was easily accomplished. By October 15th she had increased to 53 pounds, and she also increased in height.

Case VI.—Female. American. Age three. First seen October 10, 1921. Height 3 feet, 4½ inches on admission. Weight 30 pounds.

The father and mother are living and well. A great-grandmother on her father's side had diabetes. A sister developed diabetes at the age of seven, and died of pneumonia at the age of ten. During the last year of life the diabetes was of the severe type, and was controlled only with closely restricted diet.

The past history was negative. The mother had always deprived her of sugar, pastries, and high class carbohydrate foods on account of the family history of diabetes, and had kept her body weight normal. She was always active and strong. Physical examination was negative.

The history of the case was that three days before admission she had abdominal pain and cramps, without fever, thirst, or polyuria. The mother found sugar in the urine, and its presence was verified by the family physician. Carbohydrate was restricted and the urine was found negative on the two following days.

A blood-sugar on admission (October 10, 1921) was 112 mg. per 100 c.c. Glycosuria was absent. A higher plasma sugar of

146 mg. per 100 c.c., without glycosuria, was noted after a heavy carbohydrate meal the following day.

A glucose test was performed on October 12th; 30 grams of glucose by mouth produced faint glycosuria and marked hyperglycemia. The results of the test, with subsequent data, are given in Table V. The dose of 30 grams represents 2 gm. per kgm. body weight. One-half hour after its administration the plasma sugar increased rapidly to 250 mg. per 100 c.c. At the one-hour period it was still elevated to 214 mg. per 100 c.c., and the urine was positive for sugar, the test being confirmed by the fermentation test. At the end of two hours sugar had disappeared from the urine and the blood-sugar had decreased to 126 mg. per 100 c.c.

TABLE V.—CASE VI

Date.	Plasma sugar mg. per 100 c.c.	Urine vol. c.c.	Urine dextrose reaction.	Remarks.
October 10, 1921.	112	...	Negative.	During digestion.
October 11, 1921.	146	...	Negative.	After heavy CH meal.
October 12, 1921.	...	30	Negative.	30 gm. glucose by mouth (2 gm. per kgm. body weight).
	250	...	.....	½ hour after glucose.
	214	10	V. feet.	1 hour after glucose.
	126	125	Negative.	2 hours after glucose.
December 31, 1921.	118	...	Negative.	After lunch.
March 1, 1922.	136	...	Negative.	During digestion of heavy CH meal.
August 2, 1922.	150	...	Negative.	During digestion of heavy CH meal.
November 22, 1922.	152	...	Negative.	During heavy CH meal.
November 23, 1922.	90	125	Negative.	35 gm. glucose by mouth (2 gm. per kgm. body weight).
	272	...	.....	½ hour after glucose.
	268	11	V. feet.	1 hour after glucose.
	137	105	Negative.	2 hours after glucose.
	50	255	Negative.	3 hours after glucose.

The case was diagnosed as one of potential diabetes, the mildness of the case probably being due to the fact that it was hereditary in type. The mother was advised to take precautions and give the child a diabetic diet of liberal amount. Sugar was to be avoided entirely, and bread and cereals used only occasionally. Protein was not to be restricted, but the total caloric value of the diet was to be kept low.

The child was next seen December 31, 1921. Neither her height nor her weight had increased. The diet had been fol-

lowed carefully, and several urine tests performed by the mother were found negative for sugar. A blood analysis made an hour after her lunch was found to be normal, namely, 118 mg. per 100 c.c.

She was next seen March 1, 1922. The diet had been of low calorie type. Occasionally small amounts of cereal and bread were used. At no time did she use sugar. A blood specimen taken during digestion of the noon meal was found to be 136 mg. per 100 c.c. Glycosuria and acetone were negative. The height had increased to 3 feet, 5½ inches, but the body weight was still 30 pounds. The mother was instructed to increase the diet.

On August 2, 1922 she again reported for examination. Her height had increased to 4 feet, 6 inches, and her weight to 33 pounds. She was not undernourished in appearance. She was active and had no complaints. Her diet had averaged from 100 to 150 grams of carbohydrate daily, with unrestricted protein, and with moderate fats. One hour before reporting for the blood test she was given a heavy carbohydrate meal, including 1 slice of bread, 1 peach, carrots, and 1 teaspoonful of sugar. The blood analysis was found to be 150 mg. per 100 c.c., but the urine was negative for sugar and acetone.

On November 22d she was seen at office call. Her mother had previously been instructed to give her a heavy carbohydrate meal. A specimen fifty minutes after the meal was completed showed slight hyperglycemia of 152 mg. per 100 c.c. From the time of the last previous office call the diet had gradually become more liberal, due to addition of higher class carbohydrate foods. She had bread and cereal daily, but never sugar. Her weight had increased to 35½ pounds, and the height to 3 feet, 6½ inches. She was well nourished, but not especially overweight. For two weeks previous to her visit she had severe bronchitis, which was worse at night; occasionally she had slight fever.

In November a second glucose tolerance test was performed in the presence of the existing infection; 2 gm. of glucose per kgm. body weight was given just as in the previous test. A fasting plasma sugar before glucose was administered was found

normal, namely, 90 mg. per 100 c.c. Thirty minutes after glucose was administered the plasma sugar increased rapidly to 272 mg. per 100 c.c., and remained elevated to 268 mg. per 100 c.c. at the end of the hour period. A faint trace of sugar appeared in the urine at the end of the hour period. The second and third hour tests were 137 and 50 mg. per 100 c.c. respectively, without glycosuria. Acetone, albumin, and diacetic acid were absent, just as they had been on all previous occasions.

CONCLUSIONS

1. The carbohydrate tolerance of persons susceptible to diabetes, as shown by the glucose tolerance test, was studied at intervals. Tolerance was lost due to neglect of dietary precautions. Tolerance decreased with prolonged overnutrition and gradual rise in body weight.

2. Several persons with proved tendency to lowered glucose tolerance, but without frank diabetic manifestations, showed improvement in carbohydrate assimilation following application of the principle of low nutrition.

CLINIC OF DR. REUBEN OTTENBERG

MOUNT SINAI HOSPITAL

THE COURSE OF PERNICIOUS ANEMIA. THE STUDY OF ONE UNUSUAL CASE

THE case which I have to present is extraordinary. It is among the small number of very prolonged cases of pernicious anemia. The patient has received a very large number of blood transfusions, and has lived nine years since a splenectomy, performed when she had already been ill for approximately four years. Thus she is now living, thirteen years after the onset of her illness.

When I first saw the patient at Mount Sinai Hospital on February 15, 1912 she had been referred by Dr. John MacKenty (who had made the diagnosis) to Dr. Leo Buerger for blood transfusion. Dr. E. Libman took charge of the general management of the case. It is to these gentlemen, who subsequently turned the care of the patient over to me, that I am indebted for the opportunity to study so interesting a case.

At the time I first saw the patient she was thirty-five years old. As is well known, the age of onset of pernicious anemia roughly coincides with the so-called "cancer age," namely, from thirty-five years onward, and probably more of the cases occur in persons of the fourth and fifth decades than in the third.

The family history was negative, the father having died of paralysis at the age of seventy-three, the mother, of apoplexy at the age of fifty. Except for measles as a child the patient had never been ill in her life. She was unmarried. Her menstruation had always been regular and painless. There had been amenorrhea for nine months.

The present illness began in the summer of 1910, when the patient gradually became run down and very pale. Her weakness increased and she had palpitation and indigestion. Her physician recognized that she was anemic. She improved a little under treatment, but in the spring of 1911 she grew steadily worse and began to have a pronounced yellow color and to suffer much from diarrhea. In August, 1911 she commenced to show swelling of the legs, which steadily increased. At that time the diagnosis of pernicious anemia was made. For some months she had suffered with soreness of the mouth and tongue.

The physical examination was typical of an advanced case of pernicious anemia. The general nutrition was good, but there was an extreme lemon-yellow pallor of the skin and pronounced edema of the face, hands, and legs. The pupils were equal and reacted to light and accommodation. The tongue was glossy and its edges atrophied. The throat showed nothing abnormal, the teeth were fair. The lungs were normal. The heart was not enlarged. There was a systolic murmur at the base and over the vessels of the neck. The abdomen was negative except that the spleen was palpable about 1 cm. below the costal edge. There were no lymph-node enlargements. The knee-jerks were present and there were no disturbances of sensation anywhere.

The blood-count showed: Hemoglobin, 23 per cent.; red blood-cells, 800,000; white blood-cells, 4000.

Differential count: Polynuclears, 71 per cent.; lymphocytes, 23 per cent.; mononuclears, 2 per cent.; eosinophils, 4 per cent.

There was very pronounced poikilocytosis and polychromatophilia, and there were 5 normoblasts and 1 megaloblast per 100 white blood-cells. The average size of the red blood-cells was larger than normal. The color-index was 1.4.

On February 16, 1912 a direct blood transfusion by the artery-to-vein suture method of Dr. Carrel was performed by Dr. Buerger. In the direct artery-to-vein transfusion it is impossible to measure the blood which is actually being transferred. Therefore, the maximum rise in hemoglobin which could

be safely reached at one transfusion was calculated beforehand by the method described by Dr. Libman and myself in 1914.[1]

Although artery-to-vein transfusion is no longer practised clinically, and therefore this method of calculation is no longer needed for this purpose, the method is still of considerable clinical value for the purpose of estimating what improvement in hemoglobin percentage can be anticipated in a given patient from a transfusion of a given number of cubic centimeters of blood. The method is based on the simple mixture principle. Thus, if one were to mix 2 parts of any 100 per cent. solution with 3 parts of any 40 per cent. solution, the strength of the resulting solution would be easily calculated by adding two times one hundred to three times forty and then dividing the sum by the total number of parts, namely, 5. This would give a 64 per cent. solution.

This method of calculation, then, demands, in the first place, that one should know the amount of blood the patient has, as well as the percentage of hemoglobin in it. For rough, practical purposes, since there is at present no satisfactory clinical method of estimating blood volume, the blood volume is always calculated as a certain fraction of the patient's weight. Where the patient is very edematous his weight in health can perhaps be more safely taken. The estimates of the ratio of weight of the blood to the weight of the body vary between one-thirteenth and one-nineteenth of the body weight.

One-thirteenth of the body weight was assumed to be the actual ratio of body to blood. The patient had hemoglobin of 23 per cent. and weighed 130 pounds. She was, therefore, estimated as having approximately 10 pounds of blood (a pound may be taken as approximately 500 c.c.). The donor's hemoglobin percentage was 94 per cent. and he weighed 200 pounds. He was therefore estimated as having approximately 16 pounds of blood. As experimental work has shown that approximately a quarter of the body's blood may safely be removed, this was taken as the upper limit which should be transfused.

Ten pounds of 23 per cent. hemoglobin blood plus 4 pounds (one-quarter of the donor's blood volume) of 94 per cent. hemo-

globin blood should give 14 pounds of 35 per cent. hemoglobin blood, as is shown by the following calculation:

10 × 23 per cent.	= 230
4 × 74 per cent.	= 406
14 into	636 = 45 per cent.

It was therefore considered advisable to stop the transfusion as soon as the patient's hemoglobin had reached 45 per cent. This estimate was made from the point of view of the donor's ability to stand loss of blood. Crile's experimental work had made it clear that in people with normal arteries and no cardiac defect this much blood could be safely transfused. In the presence of cardiac disease or arteriosclerosis one must, of course, give much smaller amounts. As it was thought best by Dr. Libman to dehydrate the patient so as to have her actual blood volume as small as possible at the time of transfusion, she received a saline cathartic the day before, and her total intake of food and fluid consisted of 900 c.c. of milk during the twenty-four hours before the transfusion. Further experience has shown this to be a valuable procedure, particularly in patients who are edematous.

During the transfusion the hemoglobin was estimated every five minutes (by the Sahli hemoglobinometer*) and the results were as follows:

After five minutes the hemoglobin was 24 per cent.
After ten minutes the hemoglobin was 30 per cent.
After fifteen minutes the hemoglobin was 38 per cent.
After twenty minutes the hemoglobin was 41 per cent.
After twenty-two minutes the hemoglobin was 42 per cent.

At this point the donor fainted and the transfusion was stopped. The donor revived in a short while and suffered no further harm.

* Since the Sahli hemoglobinometer reads normal blood at about 80 per cent. it gives an incorrect idea of the color-index. For this reason throughout this paper all Sahli readings have been transformed by multiplying by 10/8 so as to read uniformly with other methods, such as those of Haldane, Dare, or Palmer, which read normal blood at approximately 100 per cent. In the last six or seven years of the present case the estimates have been by Haldane's or Dare's methods and have needed no correction.

(I may say parenthetically that in several thousand transfusions which I have performed or witnessed I have never seen any serious harm come to a donor.)

The amount of blood used in this first transfusion, namely, 4 pounds or approximately 2000 c.c., and, in fact, probably the amount of blood used in all of the direct transfusions in the early days (provided a good anastomosis was obtained) was very large, much larger, in fact, than is today usually considered justifiable. At present 500 to 1000 c.c. is considered a satisfactory amount to transfuse.

On February 17, 1912 the blood-count of the patient showed the hemoglobin to be 36 per cent., red blood-cells 2,300,000, white blood-cells 3500. Before her admission to the hospital the patient had run a temperature of 100° to 102½° F. This gradually diminished to normal after the transfusion. Her urine after the transfusion showed no blood or hemoglobin. The color-index was 0.78, and this color-index, of less than 1 in a case of pernicious anemia is, of course, understandable in the present instance because almost two-thirds of the red blood-cells in circulation were not those of the patient, but those of the donor. I have not infrequently seen this temporary reversal of the color-index in pernicious anemia after transfusion. The patient left the hospital a week after the transfusion in very greatly improved condition. From the second day after the transfusion she experienced a sense of well being, and her appetite, which had previously been extremely poor, again became excellent. This disappearance of gastric symptoms and return of appetite is quite common after transfusions and during remissions in pernicious anemia; the interesting thing about it is that it occurs in spite of the persistence of the achylia gastrica. Soon after her return home the patient's edema disappeared completely.

She returned for examination on March 11, 1912, and reported that she was able to go out and attend to most of her usual duties. Her blood examination on this date showed the following:

Hemoglobin 55 per cent. (Haldane's carbon monoxid hemo-

Date.	Hgl. per cent.	Red cells.	Color-index.	White cells.	Differential. P. per cent.	L. per cent.	M. per cent.	E. per cent.	B. per ct.	Normoblasts.	Megaloblasts.	
1912												
2/15	24	800,000	1.5	4,000	71	23	2	4	..	5	1	
2/16	42	Trans. by Dr. Buerger direct.										
2/17	45	2,300,000	.96	3,500								
3/11	55	2,900,000	1.4	....	68½	25	6½					
3/24	70	3,300,000	1.06									
5/2	81	4,300,000	.94	6,000								
10/10	81	4,800,000	.84	6,400	63	30	6	1	..	.....	.....	General health perfect.
1913												
3/28	77	4,200,000	.91	6,000	....	....	....	....	..	.....	.....	No abnormal red blood-cells.
4/4	70	3,700,000	1.2	9,000	67	26	2½	4½	..	.....	.....	No abnormal red blood-cells except macrocytes.
1914												
1/15	50	Trans., 1000 c.c. Lindeman's syringe method.										
1/17	65	3,150,000	1.03									
1/23	70	3,000,000	1.01									
2/19	46	2,030,000	1.1	6,200	66	31	2	....	..	.....	.....	Myelocytes 1 per cent. Many megalocytes and microcytes. Much poikilocytosis. No nucleated red blood-cells.
3/10	27	Direct very large trans.										
3/10	47											
3/17	55	2,370,000	1.1	3,400	42	48	6	4				
3/30	53	1,950,000	....	5,100	73	23	3	1	..	.....	.....	Myelocytes 1 per cent.; no nucleated red blood-cells.
4/15	35	1,800,000	1.9									
4/23	32	764,000	2.09	4,100	56	44	....	....	..	.....	.....	Macrocytes in excess; microcytes; poikilocytosis; no nucleated red blood-cells.
4/25	57	Direct large trans.										
4/30	66	Splenectomy.										
5/1	62	Direct trans.										
5/3	60											
5/7	64	2,240,000	1.4	6,800								
6/5	70	3,300,000	.66	4,700	32	52	1	3				
7/1	75	3,850,000	.97	8,800	58	38	3	1	..	.....	.....	One nucleated red blood-cell. Megalocytes; slight poikilocytosis; average red cell enlarged; numerous Howell-Jolly bodies.
9/11	75	3,690,000	1.01	7,400	42	51	7	....	..	3	.....	Howell-Jolly bodies; macrocytes; slight poikilocytosis.

1915												
1/5	85	3,200,000	1.3	8,000	60	35	5	....	..	3	.....	Small number Jolly bodies; only rare microcytes; pronounced macrocytosis, very little poikilocytosis.
3/22	100	3,660,000	1.4	9,400	53	43	2	2	..	.....	.....	No nucleated red blood-cells; no Jolly bodies; macrocytosis.
7/21	73	2,200,000	1.6	7,300	63	33	3	1	..	6	1	Macrocytes predominate; small number of microcytes and of poikilocytes; many Jolly bodies.
8/7	85	3,230,000	1.3	....	64	34	1	1	..	.....	.....	Red blood-cells very large; numerous Jolly bodies.
11/6	58	1,600,000	1.7	5,500	51	44	1	2	..	11	3	Macrocytosis, some microcytes; marked poikilocytosis and polychromatophilia; numerous Jolly bodies.
11/18	35	Transfusion, 400 c.c.										
11/27	50	2,370,000	1.06									
12/6	50	1,790,000	1.3	....	36	61	3	....	..	42	11	
12/16	50	1,760,000	1.4									
12/31	42	1,320,000	1.5									
1916												
1/8	....	Transfusion, 1000 c.c.										
1/10	55	2,610,000	1.05	....	....	....	....	....	..	.....	.....	Macrocytes, normoblasts, Jolly bodies, poikilocytosis.
1/13	52	2,500,000	1.04									
1/18	60	2,940,000	1.02									
1/29	56	2,240,000	1.2									
2/28	44	1,720,000	1.02	10,400	....	....	....	....	..	.....	.....	Macrocytosis, poikilocytosis, numerous Jolly bodies.
3/14	35	1,560,000	1.1	8,800	33	64	1	2	..	23	3	Numerous megalocytes, some granulation and degeneration, polychromatophilia.
3/25	....	Trans., 880 c.c. (syringe method).										
4/1	42											
4/8	46	2,100,000	1.09	....	61	38	1	....	..	.....	.....	Poikilocytes, Jolly bodies.
4/24	40	2,000,000	1.0									
5/8	35	1,600,000	1.09									
5/13	....	Trans., 800 c.c. (syringe method).										
5/19	42	1,720,000	1.2									
5/26	41	1,440,000	1.4									
6/12	37	1,770,000	1.04									
1917												
1/6	30	1,280,000	1.1									
2/17	....	Trans., Unger apparatus.										
6/1	....	Trans.										
6/6	33	1,600,000	1.03									

Date.	Hgl. per cent.	Red cells.	Color-index.	White cells.	Differential.					Normoblasts.	Megaloblasts.	
					P. per cent.	L. per cent.	M. per cent.	E. per cent.	B. per ct.			
1917												
8/1	....	Trans.										
10/28	37	1,700,000	1.08									
11/25	....	Trans.										
11/26	40	1,690,000	1.1	6,000								
12/18	40	1,700,000	1.1									
1918												
1/15	40	1,525,000	1.3									
3/4	....	Trans.										
3/30	33											
4/17	37	1,250,000	1.08	9,000								
7/17	30	1,000,000	1.5									
7/19	....	Trans.										
7/25	40	1,720,000	1.1									
8/3	39	1,900,000	1.03									
9/5	37	1,304,000	1.4									
9/26	30	1,400,000	1.07									
10/26	25	Trans., 750 c.c., citrate method.										
10/28	39	1,800,000	1.08									
11/29	45	1,960,000	1.1									
12/31	30	Trans., 440 c.c., citrate method.										
1919												
1/2	40	1,360,000	1.4									
2/15	....	Trans.										
3/21	63	2,470,000	1.3	6,200								
4/8	60	2,810,000	1.06									
5/1	72	3,200,000	1.1	12,000								
7/15	85	4,450,000	.95	8,800	....	....	....	....	..	.....	.....	Red blood-cells almost uniform in size and very large; no pallor at center; no poikilocytosis; no nucleated red blood-cells, but 10 per cent. show Jolly bodies.
10/21	95	4,700,000	1.01	9,700	59	40	....	1	..	6	.....	Practicaly all cells are macrocytes, numerous Jolly bodies.
1920												
2/17	91	3,680,000	1.2	10,000	72	25	3	..	..	6	.....	Macrocytosis Jolly bodies.
2/26	98	3,780,000	1.3									

1920												
4/1	90	3,000,000	1.5	6,650	71	26	3	....	..	2	.....	Macrocytosis, Jolly bodies.
6/29	85	2,200,000	1.9									
9/29	45	1,550,000	1.4	5,100								
10/6	35	Trans. citrate, 500 c.c.										
10/7	46	1,940,000	1.4	5,800								
10/21	46	2,100,000	1.09	4,900	47	50	3	....	..	.....	.....	Normoblasts, megaloblasts, poikilocytosis; polychromatophilia.
11/1	46	2,040,000	1.1	5,000								
11/6	30											
11/15	....	Trans. citrate, 1000 c.c.										
11/17	45	1,900,000	1.18									
11/29	50	2,140,000	1.16	....	45	53	2					
12/13	35	1,680,000	1.04	5,300								
12/18	....	Trans. citrate, 850 c.c.										
12/22	46	2,300,000	1.0	4,600								
1921												
1/19	38	2,200,000	0.86									
2/3	35	1,500,000	1.16	6,600								
2/10	30	Trans. citrate.										
2/11	47	1,900,000	1.2									
2/23	50	2,120,000	1.17	....	....	....	....	....	..	.....	.....	Platelets 300,000.
3/8	45	1,920,000	1.16	....	57	40	3	....	..	14	6	
3/10	....	Trans.										
3/15	50	2,220,000	1.12									
3/26	45	1,900,000	1.13									
4/27	43	1,930,000	1.11									
5/23	38	1,620,000	1.17	....	....	....	....	....	..	.....	.....	Platelets 160,000; white blood-cells and nuclear red blood-cells 9800.
7/5	33	1,530,000	1.07									
7/19	30	1,200,000	1.25									
7/26	....	Trans.										
7/27	40	1,560,000	1.28	5,300	70	28	2	....	..	1	4	Poikilocytosis, macrocytosis, megalocytosis; polychromatophilia.
8/10	42	1,795,000	1.16									
9/14	41	1,850,000	1.10									
9/24	....	.....	....	....	....	....	....	....	..	.....	.....	Attack acute pain right upper quadrant of abdomen.
10/22	30	1,400,000	1.07	4,000	34	66	....	....	..	.....	.....	Platelets 110,000.
10/29	....	Trans. citrate.										
11/2	40	1,860,000	1.08	....	52	48						
11/12	40	1,850,000	1.08	3,300								
11/22	38	1,800,000	1.05	4,400	36	62	2					

Date.	Hgl. per cent.	Red cells.	Color-index.	White cells.	Differential.					Normoblasts.	Megaloblasts.	
					P. per cent.	L. per cent.	M. per cent.	E. per cent.	B. per ct.			
1921												
12/6	35	1,580,000	1.10	5,000	55	40	5					
12/23	31	1,500,000	1.03	4,800	50	47	3					
1922												
1/3	28	1,350,000	1.03									
1/7	....	Trans., 1000 c.c. citrate.										
1/9	39	2,000,000	0.97	5,200	51	46	2	1				
1/30	39	1,850,000	1.05	5,000	52	43	4	1				
2/24	38	1,770,000	1.07	5,400	50	47	3					
4/7	35	1,430,000	1.2									
4/28	33	Trans.										
5/4	42	1,760,000	1.19									
6/23	38	1,830,000	1.03	6,900	64	34	3	....	..	.....	.....	Platelets 170,000. Normoblasts and megaloblasts abundant. No Jolly bodies.
8/8	30	1,500,000	1.0	5,200								
8/12	....	Trans., 1000 c.c. citrate.										
8/15	50	2,250,000	1.11	4,000								
9/21	42	2,000,000	1.05	6,000	....	....	....	....	..	.....	.....	Germanium injection, four injections at five-day intervals.
9/30	34	1,550,000	1.09									
10/4	33											
10/9	....	Trans., 800 c.c.										
10/13	40	2,200,000	.90	3,800	....	....	....	....	..	3	1	
10/19	42	2,100,000	1.0	3,600	....	....	....	....	..	.....	.....	Macrocytosis, moderate poikilocytosis, no Jolly bodies.

globin scale reading normals at approximately 100 per cent.: Red blood-cells, 2,900,000; color-index, 0.95; polynuclears, 68½ per cent.; lymphocytes, 25 per cent.; mononuclears, 6½ per cent.

No nucleated red blood-cells seen. There were very pronounced variations in size of the red blood-cells.

From this point on, as can be seen by reference to the table of blood-counts and to the accompanying chart (Fig. 126), the patient's general condition and blood-picture steadily improved and she went into a prolonged remission lasting nearly two years.

How rapidly this remission came on may be seen from the fact that on May 2, 1912, only two and one-half months after the transfusion, the hemoglobin percentage was already 81, the red blood-cells were 4,300,000, and the white blood-cells 6000.

During this two-year remission the patient's general health was perfect and she went about all of her ordinary activities without any consciousness whatever of being ill. Her menstruation returned and was regular in occurrence. During this time the only evidence of abnormality that the blood showed was the rather large size of the red blood-cells (Fig. 123).

In the beginning of 1914 the patient again commenced to go down hill, with weakness, palpitation, dyspnea, ringing in the ears, and gastric disturbances. On January 15, 1914 I did a transfusion of 1000 c.c. of blood by Lindeman's syringe cannula method, raising the hemoglobin percentage from 40 to 52. In spite of the temporary improvement from this transfusion, however, the patient became still more anemic, the edema returned, and she ran a temperature from 100° to 102½° F.

On March 10, 1914 a very large direct artery-to-vein transfusion was performed by Dr. Buerger. The hemoglobin was raised from 22 to 38 per cent. After the hemoglobin and red cells had again risen for about a week, there was a steady decline, and on April 25, 1914 another large direct transfusion was done by Dr. Buerger. This raised the hemoglobin from 26 to 46 per cent.

On April 30, 1914 the hemoglobin was 53 per cent., and following Eppinger,[2] whose important work on splenectomy

in hemolytic icterus and other diseases, including pernicious anemia, had appeared the year before (1913), a splenectomy was performed by Dr. Buerger.

Although the patient's condition after the operation was fairly good, it was considered safest to do another transfusion, and this was performed on May 1, 1914 by the direct method

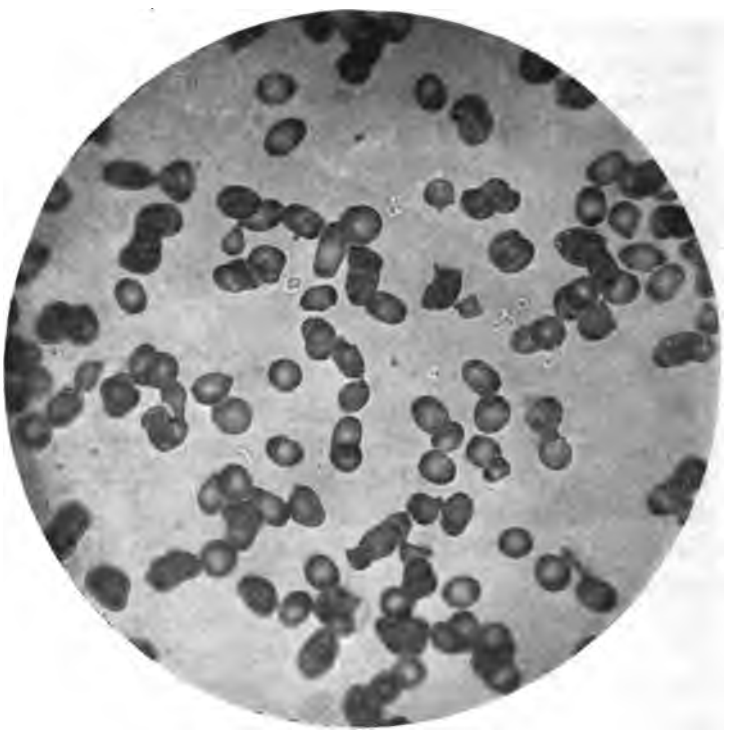

Fig. 123.—Blood of the patient (× 150) at the end of the first remission, January 8, 1914.

of Dr. Buerger. From this point on the patient made a steady recovery and was discharged from the hospital on May 15, 1914, only a little over two weeks after the operation. She at once had a remission of the disease, lasting this time a year and a half.

In spite of the fact that the patient's general condition im-

proved and that for the duration of the second long remission she appeared and felt to be in perfect health, the blood-smear showed the most extraordinary abnormalities. Thus on June 5, 1914, with a hemoglobin of 70 per cent., the smear showed 25 normoblasts and 12 megaloblasts for every 100 white cells. There were large numbers of Howell-Jolly bodies in the red

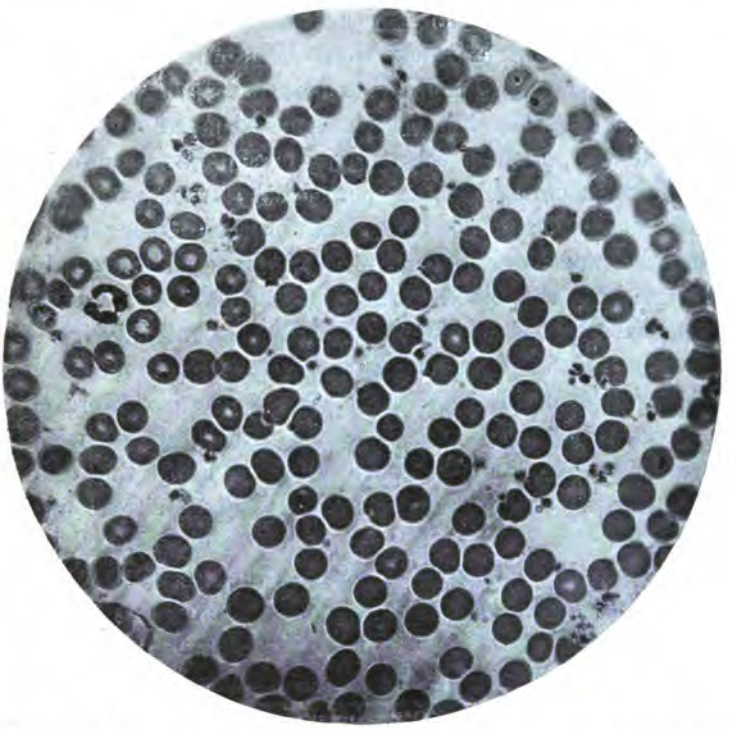

Fig. 124.—A normal blood (× 150). Contrast the size and shape of the cells with Fig. 123.

blood-cells, as well as numerous megalocytes and pronounced poikilocytosis (Fig. 124).

Although the number of nucleated red cells diminished during the year following, some of them persisted in the blood and the Howell-Jolly bodies continued to be present. In the autumn of 1915 the patient again began to go rapidly down in

health, and on November 18, 1915 I did another transfusion, this time of 400 c.c. by the syringe method. This transfusion was followed by only short-lived improvement.

For the following three years the patient continued in poor condition, and repeated transfusions (twelve in all during this period) had to be performed. It was found that until her hemoglobin percentage came down to approximately 30 per cent. she could be fairly comfortable and on her feet, provided she did not attempt any extra exertion. The general plan followed then was to make regular blood examinations and to do a transfusion whenever the hemoglobin approximated 30 per cent. After a few experiences the patient herself was generally able to tell fairly accurately when she needed a transfusion. As far as can be seen from the blood examinations during this long period, the blood-making power of the body was never able to catch up with the blood-destroying process which was going on, and each transfusion would give the patient only from one to three months of relative comfort.

Until October 26, 1918 the methods practised were either the Lindeman syringe method or the syringe method with the three-way stop-cock apparatus of Unger. From this date on all the transfusions done were by the sodium citrate method of Lewisohn, for which, after she had once experienced it, the patient expressed a decided preference on account of its simplicity. It may be mentioned that chills have occurred following a considerable proportion of the patient's transfusion whether by syringe or sodium citrate method, although they have been somewhat more frequent after the citrate transfusions. Chills did not follow the direct artery-to-vein transfusions.

In July, 1918, the question of possible focal infection in pernicious anemia having been recently raised (Barker and Sprunt[3]), the patient underwent a thorough re-examination. The throat, nose, and accessory sinuses were found clear by Dr. John MacKenty. A number of the teeth did show foci of infection and these were gradually cleared up in the following two years.

In the early part of 1919, without any obvious reason, the

patient again rapidly went into a remission of the disease which lasted nearly two years and during which her hemoglobin percentage and red blood-count were several times close to the normal. During this, as during the preceding remission, her menstruation returned and was normal. At the end of this remission she again went into a period of illness, which has lasted to the present, and a general description of which is about the same as that of the period 1916–19. Temporary improvement has followed each transfusion, but the general course of the illness has continued. The same plan as before was followed, the transfusion being done whenever the patient's hemoglobin approached 30 per cent. During this period the transfusions have been relatively large, usually 800 to 1000 c.c.

During the early part of 1922 the patient took radium emanation water over a period of three months without any effect on blood-picture or clinical condition. In September, 1922 a trial was made of the recently introduced Germanium dioxid by intramuscular injection for about three weeks, but as the patient went down hill much more rapidly during its use than during the period before its use, it was discontinued.

During all this last period the general physical examination of the patient has remained the same. The yellow color which was present before the first transfusion has never returned so intensely since the splenectomy, although the patient's skin shows a certain amount of brownish pigment.

There is at times slight edema of the eyes or the ankles. All the nerve reflexes have remained normal and the general nutrition fairly good. The patient has continued on her feet practically all of the time. She has taken hydrochloric acid in rather large doses after meals continuously except during a few recurrences of glossitis. She has had only occasional and slight attacks of diarrhea. Her blood-picture has remained extremely abnormal, but the number of nucleated red blood-cells and of Howell-Jolly bodies has become much smaller than it was in the first attack after the splenectomy (Fig. 125).

Let us now look over the chart which represents the hemoglobin percentage of the patient at the different blood examina-

tions (Fig. 126). Since the actual percentage of hemoglobin is the most important factor in determining the respiratory function of the blood the chart of the hemoglobin percentages is the best index of the course of the disease.

As we summarize with this chart before us (Fig. 126), we see that we have a patient who is still alive, and who, although

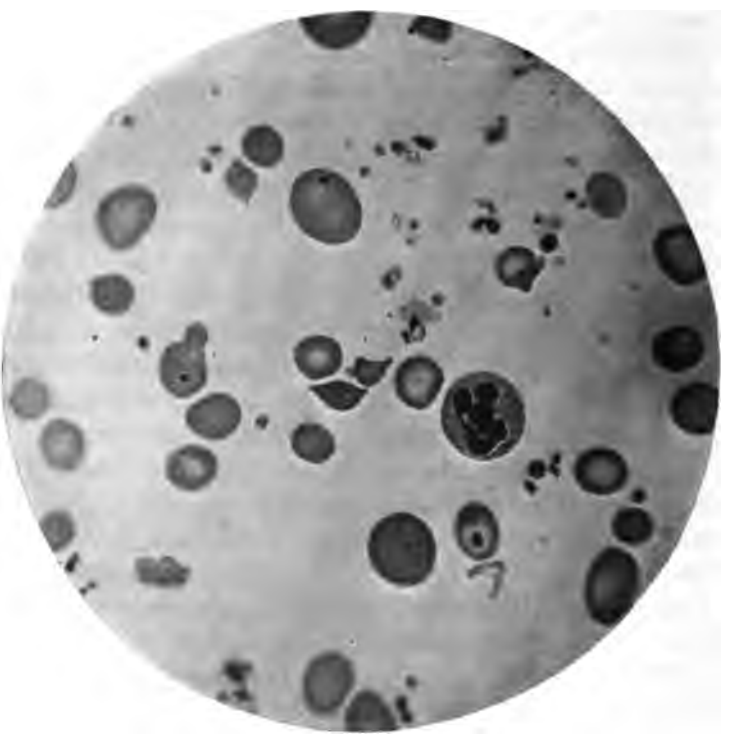

Fig. 125.—Blood of the patient March, 1919 (× 350), showing Howell-Jolly bodies, macrocytes, microcytes, and poikilocytes.

not well, is fairly comfortable after having pernicious anemia for thirteen years. During the last eleven years I have been able to follow the course of her illness very closely. At the onset she was very desperately ill, and except for the absence of nervous symptoms (such as parethesia, anesthesia, ataxia, or men-

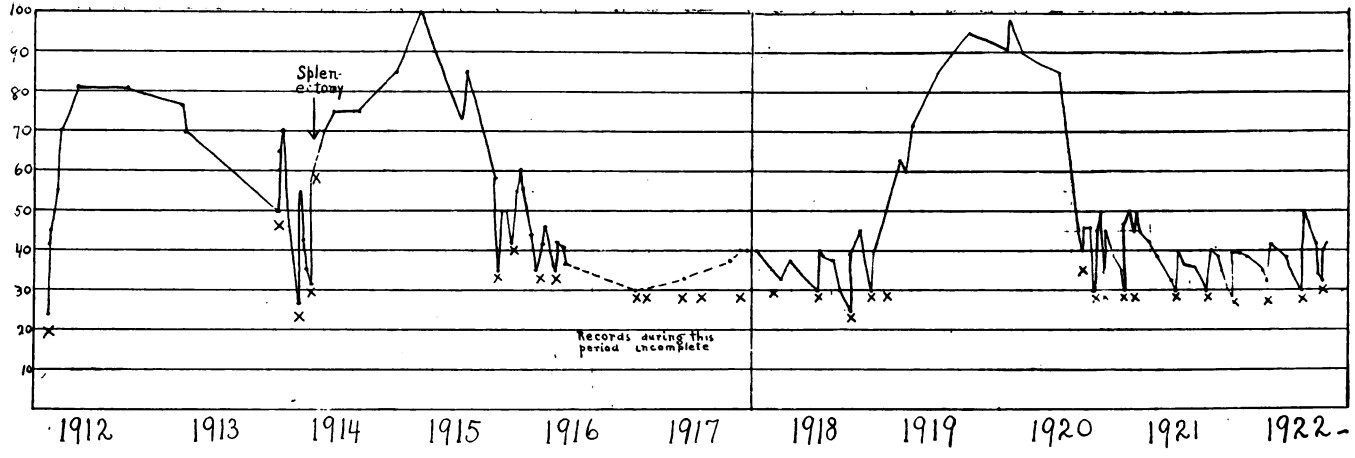
100
90
80
70
60
50
40
30
20
10
Splen-
e-tomy
Records during this
period incomplete
1912
1913
1914
1915
1916
1917
1918
1919
1920
1921
1922-

Fig. 126.

tal disturbances) she presented the appearance of the most acute and progressive type of the disease.

She has had thirty blood transfusions and has had her spleen removed (after four years of the disease). The total amount of blood which she has received from other persons is over 25 liters.

The course of the illness shows three long remissions of from one and a half years to two years in duration, of which the first followed immediately after the first transfusion (which was very large), and the second followed immediately after the splenectomy, while the third did not follow any change in treatment or environment which we can account for. The disease (that is to say the enemic and ill periods of it) consists of three long attacks and one short attack.

It may now be profitable for us to go back and discuss separately certain points of interest which are brought up by a consideration of the case.

The duration of this case as compared to the duration of pernicious anemia in general is long.

Cabot[4] (in a study embracing about 1200 collected cases) shows that the disease is usually fatal in from one to three years. Any case that lasts over four years is considered an unusually long one. Cabot himself has records of 37 very protracted cases, of which 9 lasted for ten years, 3 for eleven years, 2 for twelve years, and 3 between fourteen and fifteen years. Aside from these, there is a case reported by McPhedran[5] in which a patient with a probable pernicious anemia underwent a remission lasting seventeen years and again developed the disease and died of it, and there is a similar case reported by Stockton[6] in which a remission of twenty years was followed by recurrence of the disease.

The number of cases of longer duration than the case under consideration is exceedingly small in proportion to the total number of cases. This is the only one of the protracted cases reported in which special efforts, such as the splenectomy and the blood transfusions, were made to keep the patient alive.

The question arises as to whether the long course was actually

due to the splenectomy or to the transfusions, or whether the patient would have run this course without this interference. It is a question that cannot be settled by reference to this one case alone, but nevertheless this case offers something to the solution of the general question. It is well known that the course of pernicious anemia is marked by remissions and that they may occur without any known inciting agent. Nevertheless, the prompt onset of a remission after the first transfusion was so striking that it confirms the impression gained from observation of a good many other pernicious anemia cases, that a transfusion increases the patient's chance of undergoing a remission.

The same thing may be said of the splenectomy. The patient was doing so very badly before the splenectomy that the prompt onset of the remission after splenectomy cannot fail to give the impression of a casual connection. This, of course, is in accordance with the observations of other writers. Whether the splenectomy has had any effect on the further course of the disease since the remission which immediately followed it is more difficult to say. Certainly, the permanent influence of the splenectomy may be seen in the blood-picture; for during all the years since the splenectomy the blood has borne the earmarks of postsplenectomy blood. The number of Howell-Jolly bodies (which so characteristically appear after splenectomy) gradually decreased during the four or five years following the splenectomy, but some of these bodies appear in the blood up to the present. One striking difference in the patient's appearance has been permanent since the splenectomy. Even when she has been as anemic as she was before the splenectomy, her complexion has never been of the extreme lemon-yellow color which it showed when she was very anemic before the splenectomy.

During the first long period of illness, which followed the postsplenectomy remission and lasted during 1916, 1917, and 1918, it appeared that the transfused blood was "held" longer by the patient, or at least the patient did not go down hill as rapidly after the transfusions as is usually the case in pernicious

anemia. During the recent period of illness, however, (during 1921 and 1922), this has not been the case. It seems possible, therefore, that the longer holding up of red cells and hemoglobin percentage after the transfusions of the first long period represents the influence of the splenectomy.

It might be asked, "Was it worth the patient's while to undergo this long course of transfusion and be kept alive by the transfusions?" The best answer comes from the patient, and she herself thinks so. There is no doubt that the intelligence and fighting spirit of the patient in the present instance has helped much to keep her alive. She knew the nature of her illness practically from the beginning and held her physicians to an agreement to do their utmost to keep her alive as long as she was willing to make the fight. During the three long remissions (a total duration of about five years) she was, to all intents and purposes, in normal health. During the periods of illness she has most of the time been well enough to be up and about. In fact, she has been a bed patient only during the few recurrences of intestinal symptoms. It is true that during these periods of illness her activities were limited. Whether transfusion prolongs life or not, it certainly makes the patient more comfortable while alive. I think that patients who have been anemic for a long time grow accustomed to the anemic state, and handle themselves with reference to it much as those who have been crippled for a long while get about better than the recently injured.

The patient has come to regard transfusions as an ordinary therapeutic measure to be used when needed, like any other therapeutic measure, and this, it seems to me, is correct. The entire laity and many doctors who are not very familiar with transfusion regard it as an emergency measure, to be used only in the most desperate cases and then as seldom as possible because they believe it to be ineffective and rather dangerous. The fact is that temporary symptomatic relief from a properly carried out transfusion may practically be promised in most cases of pernicious anemia. Accidents and serious consequences from transfusion are becoming more and more rare as the proper

selection of donors by the blood-group tests is becoming better and better understood. I have recently written an article[7] describing the sources of error and the best technic of this test, and it is very important that donors of the correct group be chosen.

In none of the 30 transfusions which the patient has undergone has there been any symptom of blood incompatability or any serious reaction. During the first five years of the patient's transfusion life the blood of the donor was always tested for incompatability by direct test against the blood-serum and cells of the patient. During the last six years reliance has been placed entirely on the group test, and when a transfusion has become necessary I simply have sent for another donor of the patient's group (Group II).

In the present case splenectomy seemed to exert a beneficial influence. Is splenectomy, however, to be advised in all cases of pernicious anemia? And if not, in what cases is it advisable? This is not the place to review the literature, but the favorable reports of Eppinger,[8] Minot and Lee,[9] Haggard,[10] Klemperer,[11] Percy,[12] and Giffin[13] show unmistakably that splenectomy, although a dangerous operation in itself, has, without doubt, a favorable influence on the course of the disease and frequently initiates a remission. The only completely unfavorable report on splenectomy is that of Bloomfield,[14] of Baltimore, who, in his 8 splenectomy cases concluded that there was no change in the clinical picture and no prolongation of life. There is no doubt, however, that splenectomy should not be done in every case of pernicious anemia. It should not be done in old or greatly enfeebled persons; it should not be done in patients who have already developed any of the neurologic symptoms of the disease, since experience has shown that splenectomy (as well as transfusion) has no effect whatever on these symptoms which are usually steadily progressive and overshadow the anemia itself (Haggard[10]). Splenectomy should not be done on any patient at a time when the anemia is grave. The blood must always be improved by one or more transfusions until the hemoglobin percentage is at least 50 or 60 per cent.

before the splenectomy can be undertaken with anything like safety. It is frequently stated (although, it seems to me, without sufficient justification) that the evidences of hemolysis, such as pronounced yellow color of the patient, the presence of bile in the blood, or of much urobilin in the urine and stools, are the necessary indications for splenectomy. All cases of pernicious anemia are cases in which the blood is being destroyed rapidly, and the presence and amount of pigments are dependent on so many complicated factors that it does not seem to me we are yet in a position to use them in determining whether the case is one that requires splenectomy or not. The same may be said of enlargement of the spleen as an indication for splenectomy. There is no real evidence yet that the cases in which the spleen is enlarged are those in which splenectomy is likely to do good.

In the histology of the blood in this case there are a number of incidental observations worth mentioning. The numbers of lobes of the nuclei of the neutrophilic leukocytes (as first observed by Arneth and reported on by Briggs[15]) were increased from the first. This occurrence of five to seven lobes in the polynuclear cell as compared with the predominant two to four lobes in normal blood is believed to be an indication that the leukocytes in question are old; that is to say, they have been held in the circulation for a longer time than normal, and this, in turn, is believed to be a result of the slow production of the leukocytes by the bone-marrow in the disease. The leukopenia, which is characteristic of the disease and which has been present throughout this case whenever the patient was not doing well, is another expression of the same process. The changes in the blood following splenectomy in this case are those which have been reported in almost all the cases in the literature. The great numbers of normoblasts and megaloblasts, numerous Howell-Jolly bodies (small round granules evidently of nuclear origin present in the red cells) have been described in practically all the cases of splenectomy done for pernicious anemia. The mechanism of these changes is not understood (Fig. 127). They occur to a much less extent in

splenectomy for other causes. In the present case the size of the red blood-cells has undoubtedly been larger since the splenectomy than before, but it is not certain whether this is due to the splenectomy or merely to a long duration of the case.

The peculiarities of the blood-pictures during the remissions are of considerable interest. During the first remission

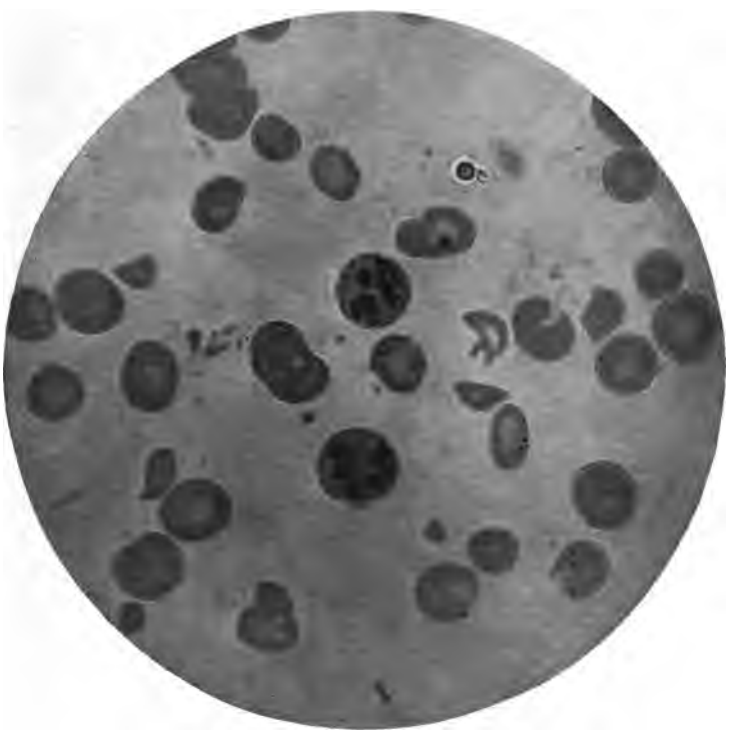

Fig. 127.—Blood of the patient in the third remission. Note the extreme macrocytosis and the multiple lobes of the nuclei of the leukocytes.

(before the splenectomy) all the blood-cells were of practically uniform size and were unmistakable larger than normal. There were no nucleated red blood-cells and no other abnormalities were observed.

During the second remission which followed the splenectomy, although the hemoglobin percentage approached the

normal, there were large numbers of nucleated red blood-cells and Howell-Jolly bodies, and the variations in size of the cell (anisocytosis) were very marked.

The blood-platelets were not counted until recent years. Within the last three years, however, they have generally been from 100,000 to 200,000, slightly below the normal range of 200,000 to 400,000. It is well known that the platelets are increased after splenectomy and that they are much reduced (usually below 100,000) in cases of pernicious anemia.

As to drug therapy, during the first attack of the disease and at irregular periods in the subsequent course of the disease, arsenic, chiefly in the form of Fowler's solution, was tried. It has never seemed to have any effect whatever on the course of the disease in this case. The unsuccessful use of radium emanation and of Germanium dioxid was mentioned above. Since the splenectomy the patient has continually taken diluted hydrochloric acid in doses of from 15 to 30 minims after meals, and she herself attributes her relatively good digestion to this medication. It seems possible that her freedom from the diarrheal attacks, which caused her most acute suffering in the early stage of the disease, may be due to the hydrochloric acid. The intestinal disturbances so common in pernicious anemia are, to some extent at least, the result of the achylia gastrica, which is known to occur in practically all cases of pernicious anemia. Chronic diarrhea is one of the well-recognized results of achylia gastrica, even in the absence of pernicious anemia.

The patient is still alive and able to attend to her household duties after having had pernicious anemia for thirteen years. This is probably, although not with absolute certainty, the result of 30 blood transfusions and a splenectomy.

In my treatment of the disease the most efficient measures have been the continuous administration of hydrochloric acid and the persistent performance of large blood transfusions. Transfusions should be regarded as a routine and relatively simple procedure, and when properly carried out should be without danger. The statement has been made very often that in pernicious anemia small transfusions are as good as

large ones. This does not seem to me to be the case. In the first place, the majority of the transfusions are of benefit solely by their symptomatic effect. They provide a patient with what he needs—more blood. And up to the patient's point of tolerance and the donor's ability to give blood it seems to me that the more blood transfused, the better. In the present and in other cases the occurrence of remissions does not seem to bear any relation to the size of the transfusion. It is true that a very large transfusion was done before the first remission, as well as before the second remission, but, on the other hand, in the later course of the disease, as well as during the period just prior to splenectomy, a number of very large transfusions were done and were not followed by remissions. There were also a number of small transfusions (400 to 500 c.c.) which were not followed by remissions. It seems to me that if a transfusion initiates a remission (and possibly the same may be said of splenectomy) it is because the transfusion in some way upsets the unfavorable balance between blood destruction and regeneration. It is conceivable that it may do this by giving a temporary rest to the blood-making function (in much the same way as in diabetes temporary rest of the sugar metabolizing function actually increases the sugar metabolizing).

Unless one throws up his hands and says that since this is an incurable disease there is no use treating it, there is another and important argument for frequent and large, rather than half-hearted and occasional, transfusions. Prolonged severe anemia results in functional impairment of the important organs (as Christian showed with regard to the kidneys) and in wide-spread fatty degeneration of the viscera, particularly of the liver. If we are to do anything for the patient at all the indication would seem to be to relieve the anemia so far as we can whenever it becomes pronounced enough to interfere with the respiratory function—the most easily observed of all the great vital functions.

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CLINIC OF DR. HENRY ALSOP RILEY

NEUROLOGICAL INSTITUTE

CORTICAL ANESTHESIA

ANESTHESIA depends upon a solution in continuity between the individual's consciousness and the stimuli resultant from contact with the environment. In the broad sense it applies to all types of general and special sensibility, but in the usual acceptance of the term it is applied to the sensations which are received from the body tissues, superficial and deep. The interference with the proper appreciation of sensory impressions may take place at any point between the peripheral end organs and the receiving stations in the brain, and even higher than that, in the actual mechanism of consciousness itself. The criteria by which we may determine the site of the lesion producing this interference in the conduction pathway depend in great part upon very careful sensory examinations and the analysis of the material obtained by definite methods of procedure. The data obtained in the anamnesis is often of material value in differentiating between varying types of anesthesia, but the objective investigation of the patient supplies much more definite and valuable evidence than his subjective sensations. It is often remarkable to find but little subjective disturbance in cases of extensive and severe sensory change, large patches of anesthesia to all types of stimuli, and dissociations, with complete loss of some with retention of other forms of sensation having completely and probably for considerable periods escaped detection by the patient.

The main emphasis in differentiating disturbances in sensibility is to be placed upon the anatomic distribution of the changes found by physical examination and the analysis of the type of interference present in each individual case.

Disturbances in sensibility fall into two large groups—the functional and the organic. A differentiation between these

two groups must be made at the onset in the determination of the character of any sensory disturbance. This distinction is vital in all neurologic diagnosis and must precede any further attempt at investigation. Functional disturbances in the sensibility are of tremendous importance. In frequency they probably exceed all other manifestations of function disturbances in the nervous system.

ANESTHESIA DUE TO CORTICAL LESIONS

The case histories of the 4 patients which are detailed in this connection seem to exemplify the disturbances in sensibility which follow lesions in the cerebral cortex itself. Two of the cases, A. N. and J. H., were operated upon for the relief of their symptoms, and the pathologic area was laid bare for direct ocular investigation. J. P. was operated upon for the relief of his symptoms, which indicated an involvement of an area further cephalad than the region given over to the cortical elaboration of the various elementary types of sensibility, and only postoperatively, as a result of circulatory disturbance, did he develop the disturbances which were considered definite enough to indicate an interference with the function of the parietal lobe of the brain. The fourth case, E. C., was observed only clinically, and the determination of the locus of her lesion depended upon the results of clinical diagnosis only. Her symptoms were, however, so definite and symptoms indicative of the involvement of other areas so conspicuously lacking that the diagnosis seems definitely justified even without exact demonstration and proof. Three of the cases, A. N., J. H., and J. P., were observed on the service of Dr. Frederick Tilney at the New York Neurological Institute, while E. C. was studied at the Neurological Department of the Vanderbilt Clinics, New York City. The case histories follow:

CASE I

Mrs. J. H., aged fifty, married; American housewife. Admitted to the New York Neurological Institute.

Present Illness.—*Chief Complaints.*—Pain in back of head; paralysis of the left arm.

Character of the First Symptom.—Headache and paralysis of left arm.

Date of First Symptom.—November, 1920.

Onset.—Sudden.

Progress of the Disease.—Characterized by remissions.

The present illness began about one year ago with a pain which appeared first in the back of the head on the right side and extended forward over the right eye. The pain was sharp, localized, and did not radiate except as indicated in the complaint. The pain was present almost constantly and was fairly definite in character, subject to exacerbations, and would continue indefinitely unless relieved by medication. The pain was entirely relieved by moderate doses of aspirin. Exposure to cold, especially riding in an automobile, made the pain much worse. The sinuses were examined and nothing pathologic, sufficient to explain the condition, was found. The pain was relieved by nasal irrigations. It was not affected by sneezing, coughing, or by moving about, and was so intense as to be incapacitating unless relieved by medication. She has had no vomiting, dimness of vision, or diplopia.

During the summer of 1920 the headache ceased for a time. In November, 1921, toward the end of the month, the headache, without any apparent cause, returned and spread over the right side of the head and down into the neck. This pain caused the patient to press the hand on the back of the neck and head constantly, where, by exerting some pressure, she could partially relieve the pain. One morning while dressing she found that her left hand was weak and that there was difficulty in using the fingers of the left hand, although she could move the arm, hand, and fingers. This difficulty in using her hand increased and she had to be assisted in dressing. This lasted for a day or two and then cleared up completely. The headache, however, still continued. During the Christmas holidays of 1921 the weakness and limpness of the left arm returned and has slowly progressed. She can lift her arm, move it to a certain

extent at the elbow, but she has no ability to move the wrist or the fingers.

About January 8, 1922 there was an increase in all the symptoms, so that she felt quite ill, as if she had eaten something which disagreed with her, and she was confined to bed. A few days later *x*-rays of her teeth and sinuses were taken, which were quite negative. At that time she noticed also that there was some numbness in the left hand. She has had no vomiting, no trouble with her lower extremities except for a certain amount of unsteadiness in walking, which developed about the first of January. She now feels weak in her legs, but not particularly unsteady. At the time of the second attack of paralysis of the left hand a urine specimen was examined and some albumin was found, on account of which she was put upon colon irrigations.

Past History.—She has had no accidents, operations, or injuries of any severe extent. Some years ago she ran into a door and struck her head, the right side being injured, but she suffered no sequelæ from that accident. She has had no pulmonary, cardiac, or gastro-intestinal symptoms at any time. She had measles and scarlet fever in childhood.

Personal History.—She drinks tea and coffee in moderation. She does not use alcohol or tobacco. She sleeps well. Her appetite is good, bowels move regularly, and there has been no marked loss or gain in weight recently. There has been no disturbance in urination. She has to get up to urinate once or twice every night. Her periods have been regular until two years ago, at which time she passed through the menopause. She has had 5 children, whose ages at the present time range from thirteen to four years of age; all are living and in good health, no children have died. There has been one accidental miscarriage, some years ago.

In 1910 she had a sudden disturbance in consciousness. She felt very drowsy and was said to have given a gasp and fallen to the floor, with some frothing at the mouth. She was apparently out of her head for some few hours and in bed for some days following this attack. She had recovered completely

by the following morning and did not feel particularly badly, but felt as if there had been some memory defect and as if she had been away. This attack was declared to be due to a renal disturbance.

In 1913, while abroad, after a rather long, strenuous walk she returned feeling quite exhausted, and then suddenly fainted. She felt quite ill for several days following this attack; had no appetite, stayed in bed, but did not consult any physicians.

In the autumn of 1918 she returned to her home one evening feeling quite badly. She had some nausea and felt as if she were about to vomit. She fainted. Upon returning to consciousness she had no recollection of the events immediately following her syncopal attack, but this was not followed by any other further disturbance. She was seen by a physician during this attack, but does not remember any diagnosis having been made. None of these attacks left any weakness, numbness, or any sequelæ which were of sufficient severity to attract her attention.

Physical Examination.—*Abnormal Attitudes and Deformities.*—Patient is a poorly developed, fairly nourished woman of about fifty years of age, lying quietly in bed and presenting a slight left facial weakness which is evident both in repose and in movement. She does not move her left arm spontaneously, doing everything which is possible with the right hand and arm.

Gait.—Her walking shows the results of having been confined to bed, but presents no particular weakness or unsteadiness either on one side or the other.

Co-ordination.—Equilibratory.—There was some swaying with the eyes open; not increased by closing the eyes, which seems to be the result of general, not of focal, weakness.

Non-equilibratory.—The *finger-to-nose* test was performed normally on the right side, but is quite impossible with the left hand on account of the motor weakness.

The *finger-to-finger test* was performed normally with the right hand, but is quite impossible of performance with the left hand.

The *heel-to-knee test* was performed normally in the right

leg, but presents a certain amount of ataxia and unsteadiness in the left leg. In attempting to run the heel along the shin she succeeded very well with the right leg, but presented the same ataxia and wavering movement in the left leg.

The *toe-to-object-above-the-patient test* was performed normally on the right side, but presented some weakness on the left side.

Dysmetria.—There was no dysmetria; she had no difficulty in making movements with the right hand, but efforts to test this in the left hand were impossible on account of the motor weakness.

Adiadokokinesis.—Movements intended to test the ability of patient to perform successive movements showed no impairment of cerebral function on the right side, but were impossible of performance on the left side on account of the motor weakness noted above.

Skilled Acts.—These were performed normally on the right side, but could not be done with the left hand at all.

Reflexes (deep):

	Left.	Right.
Jaw	2	2
Pectoral	3, with clonus	2
Biceps	3	2
Triceps	3	2
Radial	3	2
Ulnar	3	2
Wrist	3	2
Suprapatellar	2	1
Patellar	3	2
Achilles'	3, with transient clonus	2
Periosteal, crossed and uncrossed	0	0

Reflexes (superficial):

Ciliospinal	±	±
Supra-umbilical	0	0
Suprapubic	0	0
Upper lateral abdominal	0	0
Lower lateral abdominal	0	0
Babinski	+	0
Chaddock	+	0
Oppenheim	0	0
Gordon	0	0
Schaefer	+	0

Abnormal Involuntary Movements.—There were no abnormal involuntary movements.

Muscle Strength.—Movements at the left shoulder were weak, but the shoulder could be raised to a very slight extent in all directions, and the arm could be raised forward, laterally, backward, abducted, adducted, and rotated to a very slight extent. The movements of the forearm on the arm presented extensive motor weakness both in flexion and extension. Movements of the hand on the forearm were entirely abolished and there were no movements in the fingers of the left hand whatsoever. There was some weakness in the lower extremities. Movements of the thigh on the pelvis, leg on the thigh, and the foot on the leg all presented definite weakness.

Muscle Status.—There was some atrophy of the left arm and finger muscles, although this was not of any great extent. The muscle tone was somewhat increased in the forearm and finger muscles.

Abnormal Associated Movements.—No abnormal associated movements could be elicited in tests made on the upper extremity.

General Sensory Examination.—Touch: Perception of cotton-wool was, to all intents and purposes, normal throughout the entire body, there being no definite difference in the right and left hand. Tactile localization: This quality of sensibility was considerably disturbed. Efforts to localize points stimulated on the surface of the left forearm and hand led to the production of errors about twice as extensive as those in locating similar points stimulated on the right forearm and hand. In using the two-point test it was found necessary to spread the points of the calipers about twice as far for tests on the left side as for tests on the right before the duality of stimulation was recognized.

Pain: This type of sensibility was essentially normal throughout the entire body, although the patient stated that the pin-point was not quite so definite, was somewhat more diffuse, less easily recognized on the left hand than on the right. When the pin-point was applied with the eyes open the patient said that

there was apparently some delay in the detection of the stimulus when the left side was tested, which was not present on the right side.

Temperature: This type of sensibility presented the same disturbances as those outlined on examination of the pain sensibility.

Vibratory: This sensibility was normal throughout the entire body.

Muscle tendon: This was normal in the entire body with the exception of the left upper extremity. The disturbance in this type of sensibility was most marked in the fingers, less marked at the wrist and elbow, and only slightly interfered with at the right shoulder.

Stereognosis: The ability to recognize an object by its form was absolutely lost in the left hand.

Baragnosis: The ability to estimate and compare different weights was entirely lost in the left hand.

Cranial Nerves.—Olfactory nerve: When tested objectively this nerve was found to be normal and there was no history of any hallucinations of smell.

Optic nerve: Examination of the second cranial nerve showed a normal perimetry. The eye-grounds showed a slight blurring on the mesial side of each disk. Elsewhere the outline of the disk was sharp and distinct. There was no pallor seen in the nerve head, and the media, retina, and retinal vessels showed no abnormalities.

Motor oculi, trochlear, and abducens: The pupils were equal, about 3½ mm. in diameter, were round, regular in outline, and central in position. The reaction of the pupils to light, both direct and consensual, and the reactions to accommodation and convergence were normal on the two sides. The palpebral fissures were equal on the two sides. There was no ptosis or exophthalmos present. There was no strabismus on either side and there were no deviations of the eyes. Conjugated movements of the eyes were normal except for slight weakness of the right eye in converging forward. There was no nystagmus present.

Trigeminus nerve: This nerve presented no abnormalities either in its sensory or motor portions.

The facial nerve: There was some lagging and stiffness in the movement of the left occipitofrontalis and corrugator supercilii on the left side. The left orbicularis palpebrerum muscle was somewhat weak. The musculature of the left nostril, upper and lower lips, and left side of the chin was definitely paretic in action.

Auditory nerve: Examination of the auditory apparatus showed no abnormalities with either the vestibular or the cochlear apparatus. The bone and air conduction on both sides was found to be normal, and no disturbances were found upon caloric stimulation of the semicircular canals.

Glossopharyngeal, pneumogastric, spinal accessory, and hypoglossal nerves: These nerves were all normal.

Systemic Examination.—This examination showed no definite abnormalities of any kind. The pulmonary system was apparently normal. Cardiovascular system: The heart was normal in position and outline. There were no adventitious sounds and no abnormal outlines present. The cardiac rate was 80, the blood-pressure 130/80. The blood-vessels, both arteries and veins, showed no abnormalities. Gastro-intestinal, genito-urinary, and skeletal systems were normal to superficial examination.

At a staff conference held January 19, 1922 the diagnoses suggested were a vascular lesion, neoplasm, or multiple sclerosis. The location of the lesion was considered to be probably in the right parietal, supramarginal, and angular gyri regions. The patient was observed until January 28th, during which time there was no essential change in her condition. She required repeated doses of aspirin with the occasional addition of codein for her headache. She was in bed most of the time, but was up in a chair almost every day. She slept fairly well and complained moderately of headache.

Laboratory Examination:

Hemoglobin, 90 per cent.
Red blood-cells, 5,200,000 per cubic millimeter.
White blood-cells, 8500 per cubic millimeter.
Neutrophils, 77 per cent.
Lymphocytes, 22 per cent.
Large mononuclears, 1 per cent.
Wassermann: Negative.

The spinal fluid was perfectly clear. It was under normal pressure, there were no cells found, no excess of globulin; a normal amount of sugar was present. The Wassermann and colloidal gold curve were negative.

Urine examination: Color, amber; turbid, acid; specific gravity 1.020, no albumin, no sugar, no indican, a few micro-organisms, scattered and clumped white blood-cells, and some calcium oxalate crystals.

Phenolphthalein excretion, 10 per cent. first hour.
17 per cent. second hour.
27 per cent.

The Mosenthal nephritic test-meal showed small quantities with a rather high specific gravity, with some tendency of the specific gravity to remain fixed. The excretion of urea and chlorids was normal.

The patient was operated on January 28, 1922. A right osteoplastic flap was turned down, exposing the right side of the brain from a point about 1 cm. in front of the Rolandic fissure to about the caudal extremity of the Sylvian fissure. There were no changes in the structure of the bone, which, however, was quite thick in this region. The dura mater when exposed was normal in color, presented little if any pulsation, and there was no evidence of increased intracranial pressure or any abnormal changes in local contour. Upon opening the dura an extensive area of brain degeneration was found extending from behind the Rolandic area backward into the superior parietal lobule of the right side. This area became extensive behind the ascending parietal convolution, extended upward nearly to the mesial margin of the hemisphere, and downward almost to the lips of the Sylvian fissure. In its ventral and cephalic angle it presented an extension forward which passed over the Rolandic fissure, involving the ascending frontal convolution in the area

which is known to supply the right forearm and hand. This entire area was discolored, canary yellow in color, and was much softer in consistency than the normal brain which surrounded it. Scattered over the surface were thickened vessels, some of them appearing broken and presenting a considerable distortion from the normal appearance of the blood-vessels on the surface of the brain. Scattered irregularly over the surface there were three or four light brownish cysts containing small collections of fluid, and at the confluence of the various sulci and fissures

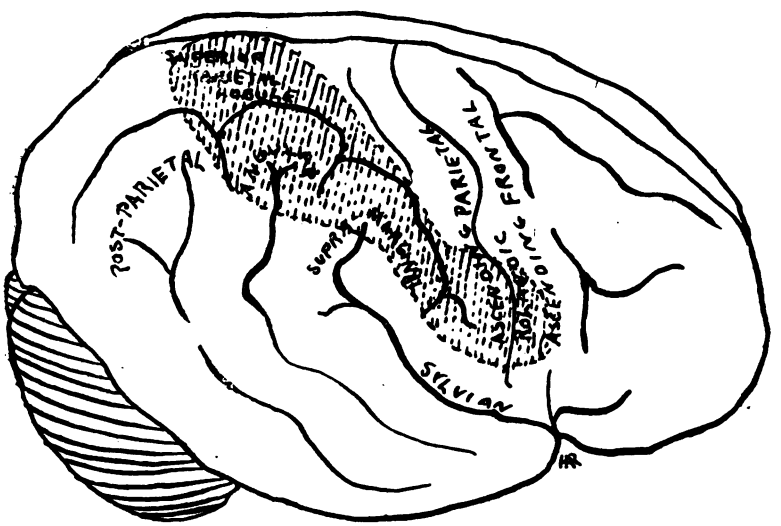

Fig. 128.—Case of J. H. The shaded area indicates the region of the cortex which was involved in the pathologic process, and shows the extension forward into the motor convolution.

the pia arachnoid was thickened and milky in appearance. The entire region presented the appearance of an advanced degeneration with cyst formation. The dura and superficial tissues were closed without further investigation and no tissue was removed for pathologic examination. The postoperative course was quite uneventful, there being no reaction and only a negligible amount of nausea and vomiting. The course since operation has been one of progressive improvement until, at the present time, there is considerable movement in the arm and

hand and some control over the fingers. There is, however, no definite improvement in the sensory examination.

In reviewing the preceding case in the light of observations made at the time of the operation it is possible to reconcile the symptoms and subjective signs with the pathology found to be present at the operation. The initial symptom which persisted throughout her entire illness and presented such salient features throughout was her complaint of pain. This pain was referred to the cutaneous distribution of the trigeminal nerve and may be attributed to meningeal irritation. It is known that recurrent branches from the ophthalmic division of the fifth cranial nerve pass backward through the sphenoidal fissure and are distributed to the dura as far caudad as the tentorium. The intense vascular changes disclosed at operation all in probability affected the overlying dural membrane and made themselves evident in pain which was referred to the predominant area of cutaneous distribution of the trigeminal nerve, namely, the face and scalp of the same side of the head. The fact that exposure to cold or other factors applied to the head aggravated the pain may be taken as evidence that the pathologic process had facilitated the passage of painful stimuli over this nerve, and impulses which, normally, would only cause moderate discomfort in this case resulted in actual pain and anguish. The observation also that continued moderate soothing pressure over the same area resulted in a diminution of the pain may also suffice as further evidence that the pain was caused by irritation of the dural branches of the fifth nerve, ameliorating influences applied to the surface distribution of the nerve tending to alleviate the results of the intracranial pathology. The extension forward of this process across the Rolandic fissure and its involvement of the hand and face areas of the ascending frontal or motor convolution readily explain the motor symptoms which were present in the left hand and lower half of the face. It is difficult to reconcile the sudden disturbances in consciousness which began in 1910 and recurred in 1913 and 1918, with the condition found to be present in the brain at the operation, but it is possible that they were vascular accidents of sufficient

severity to cause temporary disturbances without leaving any evidence of permanent interference with any of the necessary somatic functions. In all probability the genesis of the present condition was operative as far back as 1910, giving rise to transient disturbances, but only becoming severe enough in 1920 to produce the disabling effects found upon examination and the extensive pathology disclosed upon the operating table.

The physical examination presents, in brief, a disturbed motor control of the left side of the body with its greatest severity focused upon the left hand, as evidenced by the interference with voluntary movement, the atrophy of disuse in the muscles of the left forearm and hand, the exaggeration of the reflexes of the left side, and the appearance of abnormal reflexes in the lower extremity. The chief disturbances elicited were the very evident defects in the synthesizing power of the parietal cortex to elaborate out of the crude sensory impressions the concepts of form, significance, purpose and names of objects, and the faculties of estimating the localization of stimuli, the determination of the distance separating two simultaneously stimulating contacts, and the recognition of the sense of movement. These faculties are composite in character, dependent upon critical attention, capable only of being exercised by the higher conscious levels, the cerebral cortex, and depending mainly upon the stored-up memories of similarities and dissimilarities. The discriminative faculties were affected without material interference with the affective types of sensibility, that is, pain and temperature, and probably vibration.

CASE II

J. P., aged thirty-six; married; American. Admitted to the New York Neurological Institute.

Present Illness.—*Chief Complaints.*—Severe headache, diminishing vision, insomina, weakness of the right arm and leg.

Character of the First Symptoms.—Weakness and headache.

Date of the First Symptom.—April 19, 1919.

Onset.—Gradual.

Progress of the Disease.—Worse.

The present illness began in April, 1919, with repeated cramps in the fingers of the right hand while playing tennis. These cramps occurred every five to ten minutes, and were not accompanied by any loss of consciousness, but were associated with temporary voluntary paralysis. These attacks occurred every four or five weeks during that year.

In January, 1920 the patient was examined, and his condition was diagnosed as an occupational neurosis.

In February, 1920 there developed severe headache which was frontal in location, rather intermittent, and associated with vomiting. These attacks came on occasionally and lasted from twenty-four to thirty-six hours. In May, 1920 the headache had become so much worse that he consulted a nose and throat specialist, who operated upon him, but without benefit. Since July, 1920 there has been increasing headache, cramps in the right hand, and an advancing weakness in the movement of the right foot. He was examined in September, 1920 at a Brooklyn Hospital, and it was found there that he had a choked disk, greater in the right than in the left eye, a transitory weakness of the left side of the face, and increased reflexes on the right side. He was found to be serologically negative and x-rays taken of the head were normal.

Past History.—No accidents or injuries. The turbinate bones were removed in 1920. He has had no illnesses in the past of any material importance.

Personal History.—Drinks 2 to 3 cups of tea a day, does not use tobacco or alcohol. He sleeps poorly and his appetite is also poor. His bowels were regular until the past two months, since which time he has been constipated. His urination is normal.

Physical Examination.—Abnormal attitudes and deformities: There were no abnormal atittudes or deformities present.

Gait.—The gait was normal.

Co-ordination.—Equilibratory and non-equilibratory: These showed no disturbance. There was no adiadokokineses, no dysmetria, and the skilled acts were normally performed. There were no abnormal involuntary movements present.

Reflexes (deep):

	Left.	Right.
Jaw	2	3
Pectoral	2	3
Biceps	2	3
Triceps	2	3
Radial	2	3
Ulnar	2	3
Wrist	2	3
Suprapatellar	2	3
Patellar	2	3
Achilles'	2	3

Reflexes (superficial):

Ciliospinal	+	+
Supra-umbilical	+	+
Suprapubic	+	+
Upper lateral abdominal	+	+
Lower lateral abdominal	+	+
Ankle-clonus	0	+
Babinski	0	0
Chaddock	0	0
Oppenheim	0	0
Gordon	0	0
Schaefer	0	0

Muscle Status.—This was normal.

Abnormal Associated Movements.—There are none present. The spinal fluid and blood Wassermann were negative.

General Sensory Examination.—The touch sensibility is normal in all its divisions, there being no disturbance in acuity, ability to recognize or discriminate between various types of stimulation. Pain normal. Temperature normal. Vibratory normal. Muscle tendon normal.

Cranial Nerves.—Olfactory normal.

Optic: The fields of vision were normal and complete.

Fundus examination: There was papilledema present in both eyes, 2 diopters in the right eye and 4 diopters in the left eye. In the left eye there were numerous recent and old hemorrhages.

Motor oculi, trochlear, and abducens: Pupils 2½ mm., round, regular in outline, central in position. The reactions to light,

both direct and consensual, and to accommodation and convergence were normal. The position of the eyes was normal, the movements of the eyes were normal. There was slight nystagmus on extreme lateral gaze which was equal upon looking to either side.

Trigeminus nerve: This nerve was normal both in its motor and sensory divisions.

Facial nerve: There was slight lagging in the movements about the lips and mouth on the right side of the face.

Glossopharyngeal, pneumogastric, spinal accessory, and hypoglossal nerves: These nerves were all normal.

Systemic Examination.—This presented no abnormalities. The heart was normal in size, sounds were normal, blood-pressure was 100/60, and the blood-vessels seemed normal to palpation.

The patient was operated upon September 29, 1920. A large osteoplastic flap over the caudal two-thirds of the frontal lobe was raised in the usual manner. Upon opening the dura a large dural endothelioma was found lying in the right frontal lobe near the median line cephalad of the motor area. The tumor was separated without great difficulty from the surrounding brain tissue, and then was removed, the cavity washed out, closed up, and the dura, bone, and superficial tissues closed in the usual manner.

Following the operation it was found that there was a complete paralysis of the right upper extremity and of the right side of the face. There was also marked weakness in the right lower extremity. Although volitional control of the right face was lost the emotional reactions were produced perfectly normally in the right side of the face, the movements of the right side of the face in laughing being the same as those of the left. The pupils reacted well to light and accommodation.

Patient returned for further examination December 3, 1921, and at that time showed the following:

There were no abnormal attitudes and deformities.

Gait was normal.

Adiadokokinesis.—Efforts to perform repeated successful

movements were impossible in the right hand, but normal in the left.

Dysmetria.—There was considerable disturbance in the ability to measure the amount of movements and distances in the performance of voluntary movements. The performance of skilled acts was impossible in the right hand on account of awkwardness and the ungainly character of the movements.

Abnormal Involuntary Movements.—There were occasional attacks of very rapidly repeated pronation and supination of the right forearm, together with some irregular twitchings in right rectus femoris.

Reflexes (deep):

	Left.	Right.
Biceps	3	3+
Triceps	3	3+
Radial	3	3+
Ulnar	3	3+
Suprapatellar	1	2
Patellar	3	3+
Achilles'	2+	2+

Reflexes (superficial):

Ciliospinal	+	+
Supra-umbilical	+	+
Suprapubic	+	+
Upper lateral abdominal	+	+
Lower lateral abdominal	+	+
The abdominal reflexes were exhaustible on both sides.		
Babinski	0	0
Chaddock	0	0
Oppenheim	0	0
Gordon	0	0
Schaefer	0	0

Muscle Strength.—Some symmetric diminution of muscle strength in right arm and leg.

Muscle Status.—This was normal.

Abnormal Associated Movements.—These were present in the right arm and hand.

General Sensory Examination.—Touch: Acuity of tactile sensibility was slightly reduced over the right hand and fore-

arm. Tactile localization was very much reduced in the right hand, forearm, the areas in localization being about twice as large as that in the left hand.

Tactile discrimination: Circles of Weber were about twice as large in the right as in the left hand.

Pain: There was no definite diminution in the acuity of the pin prick, but there seemed greater diffuseness and less ability to recognize the point stimulated.

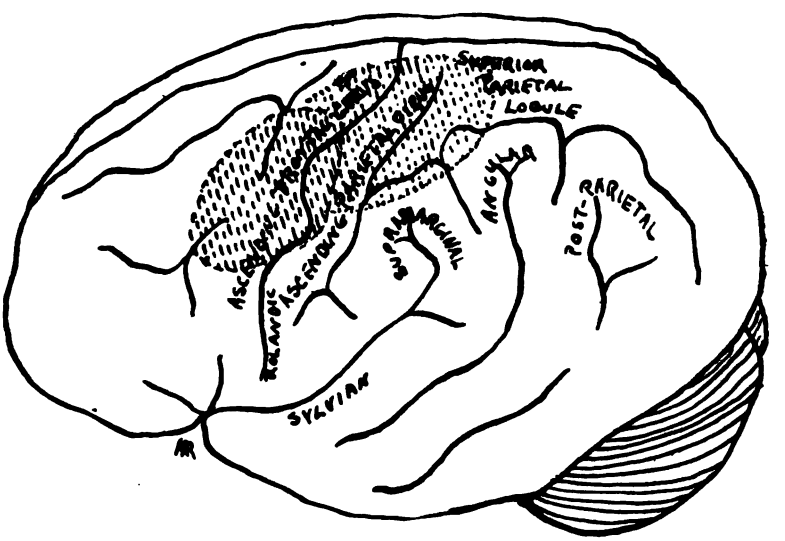

Fig. 129.—Case of J. P. The cephalic shaded area indicates the general location and extent of the tumor, while the caudal shaded area indicates the area of vascular disturbance following the removal of the neoplasm.

Vibratory sensibility: This was normal throughout.

Muscle tendon sensibility: This was very much disturbed, movement of the right fingers requiring an excursion twice as great in the right as in the left hand before the movement became recognizable.

Stereognosis and barognosis: These were both very much disturbed in the right hand.

Cranial Nerves.—These showed no particular abnormalities. Swelling of the disks about 1½ diopters in the left eye, with some

optic atrophy, was present. The pupils were equal. There is a slight motor disturbance in the right facial nerve, especially in the upper branch. There were no other disturbances in the cranial nerves.

Systemic examinations were normal.

This patient presented a perfectly clear-cut example of an expanding lesion in the left cerebral hemisphere, producing irritation of the motor cortex, with resultant spasms and increasing weakness of the right side, commencing in the foot and extending upward. The disturbances found by ophthalmoscopic examinations corroborated the other evidences of an intracranial neoplasm. The diagnosis was fully confirmed by the condition found at the time of the operation. The postoperative course presented evidences of an unusual amount of trauma incident to the removal of the neoplasm, and the development of interference with the functions of the left superior parietal lobule indicated a material disturbance in the blood-supply to that region.

CASE III

E. C., twenty-eight years of age. American; married; housewife. Admitted to the Neurological Department of the Vanderbilt Clinic, New York.

Present Illness.—*Chief Complaints.*—Loss of sensation in the fingers of the left hand. Spots on the back of the left hand.

Date of First Symptom.—March 5, 1921.

Character of First Symptom.—Fainting attack.

Onset.—Sudden.

Progress of the Disease.—Unchanging and constant.

On March 5, 1921, after having suffered from a headache of varying severity during the day, the patient went out in the evening to a theatrical performance with the idea of attempting to drive away the headache. Upon returning to her home about 11.30 P. M. she ate some shell-fish and then very suddenly felt quite dizzy and thought she heard someone at the front door. Upon investigating, she found no one there. She then sat down and suddenly fell off the chair on to the floor on account of a

sudden attack of dizziness. She did not lose consciousness, but got up from the floor and continued eating. A few minutes later she had a recurrence of the vertigo, in which she again fell from the chair to the floor. As she was still able to get up, she again seated herself, only to fall from the chair to the floor the third time. This time she found that she could not get up, but dragged herself along the floor to her bed in the next room, and succeeded in raising herself to the bed. She then noticed that there was no feeling in her left hand and she called in a physician, who gave her a hypodermic and some medicine for her nervousness. She did not sleep at all that night, and the next day she found that the condition in the left hand was about the same as it was before. On the day following the onset of her illness she suffered from some headache, but there was no dizziness. She vomited several times during that day. At that time she was two months pregnant, and examination of the urine showed that there was definite nephritic disturbance, the urine containing albumin and casts. During the days following the onset of the illness her hand was somewhat painful, but this was relieved by massage and the application of the violet ray. The fingers felt quite unnatural, being stiff, and any attempted movement was quite difficult. At the present time the main disturbance of which she complains is a loss of sensation of the entire left hand, inability to hold things, and tendency to drop things out of the hand when she is not looking directly at the object. She has noticed that she is unable to recognize objects which she holds in her hand unless she looks at the object. At no time was there any injury. She has not bitten her tongue nor has there been any incontinence.

Past History.—There have been no accidents, operations, or injuries which would have any bearing on the present condition. She has had measles three times, nephritis during pregnancy, but no other illnesses.

Personal History.—She drinks tea and coffee moderately and does not use alcohol or tobacco. She sleeps well, her appetite is good, her bowels are regular. She has no difficulty in urination and only occasional nocturia. Her menstrual func-

tion is normal, and her periods are regular, with only slight pain. She has been married seven years and has had five miscarriages, varying from the sixth to the eighth month of pregnancy. These miscarriages seem to have been definitely associated with some nephritic disturbance. She has no living children. She is left handed except for writing.

Physical Examination.—*Abnormal Attitudes and Deformities.*—There are none other than some diffuse mottling of the skin on both arms, more particularly on the left, and more extensively over the extensor surface of the left arm.

Gait.—The gait is normal and no abnormalities were brought out on any of the tests of gait.

Co-ordination.—Equilibratory.—This was normal and there was no swaying in the Romberg position.

Non-equilibratory.—Finger-to-nose test: This was performed normally with the right hand, but presented a certain amount of uncertainty and wavering in the performance of the test with the left arm.

Finger-to-finger test: In this test evidences were present of the same disturbance in approximating the left hand to the right.

Finger-to-toe test: This test was performed with precision on the right side, but presented a good deal of fumbling and awkwardness in the left hand.

Toe-to-object-above-patient test: This was normally performed.

Heel-and-knee and *along shin tests:* These were normally performed.

Adiadokokinesis.—Not present.

Dysmetria.—There was no dysmetria in the movement of the limb in general, but there is considerable difficulty in measuring the finer movements of the fingers and thumb of the left hand.

Skilled Acts.—The performance of skilled acts in the left hand was very much interfered with, whereas in the right hand all tests were normally performed. Her speech was normal.

Abnormal Involuntary Movements.—There were no abnormal involuntary movements noted.

Reflexes (deep):

	Left.	Right.
Jaw	2	2
Pectoral	2	2
Biceps	2	2
Triceps	2	2
Radial	2	2
Ulnar	2	2
Wrist	2	2
Suprapatellar	2	2
Patellar	2	2
Achilles'	2	2

Reflexes (superficial):

Ciliospinal	+	+
Supra-umbilical	+	+
Suprapubic	+	+
Upper lateral abdominal	+	+
Lower lateral abdominal	+	+
Babinski	0	0
Chaddock	0	0
Oppenheim	0	0
Gordon	0	0
Schaefer	0	0

Muscle Strength.—The muscle strength was normal except that movements in the small muscles of the left hand seemed to be weak.

Muscle Status.—In the muscle status there was apparently no atrophy or hypertrophy, and there was no change in muscle tonus anywhere throughout the body.

Abnormal Associated Movements.—There were no abnormal associated movements observed.

General Sensory Examination.—Touch: The ability to recognize cotton-wool was somewhat disturbed over the fingers of the left hand and particularly the dorsal surface of the thumb and forefinger. There was no definite anesthesia at any point.

Tactile localization: The ability to recognize the point stimulated upon the skin of the left hand was grossly inaccurate. Mistakes often of 3 to 4 inches were made in the determination of the point stimulated.

Tactile discrimination: It is necessary to separate the point

of the calipers about two and a half times as far on the left as on the right hand in order that the patient might recognize two points simultaneously stimulated. She is unable to appreciate the difference in sensation produced by rubbing the skin with fur, silk, cotton or wool, and she is unable to recognize the difference between a piece of silk and a piece of blotting-paper.

Pain: Pin prick is much more disagreeable on the left hand, and particularly the left thumb and forefinger, than on the right. The point does not feel quite so sharp on the left hand as on the right, and the stimulus appears diffused and changed in character in that the pin feels more like a hot rod. The sensation is much more diffuse and the ability to recognize the point stimulated is very much upset.

Temperature: She can appreciate the differences between the extremes of heat and cold, but cannot distinguish between the warm and cool sources of stimulation.

Vibratory: This type of sensibility is practically unchanged, although the patient complains of a painful, disagreeable quality when the tuning-fork is applied to the left hand, which is not present when the stimulation is on the right hand. Although difficult to estimate, the patient thinks that the vibration is not quite so strong on the left as on the right hand.

Muscle tendon: It is found necessary to move the thumb and index-fingers of the left hand about three times as far as in the right hand before the sense of movement is appreciated by the patient.

Stereognosis: She is entirely unable to recognize objects placed in the left hand.

Barognosis: This is practically absent in the left hand.

Acrognosis: There is a very evident disturbance in this type of sensibility, the patient being unable to appreciate the positions into which her hands and fingers were placed by the examiner.

Cranial Nerves.—Olfactory nerve: Examination of this nerve showed no abnormality.

Optic nerve: The outline of the disk was sharp and distinct, the retinal vessels and the media were normal.

Motor oculi, trochlear, and abducens nerves were normal. The pupils were equal, 3 mm. in diameter, round, regular in outline, central in position. The reaction to light, both direct and consensual, and the reaction to accommodation and convergence were normal. The position of the eyes was normal and there is no limitation of voluntary motion, and there was no nystagmus.

Trigeminus nerve: This nerve was entirely normal, both in its motor and sensory portions.

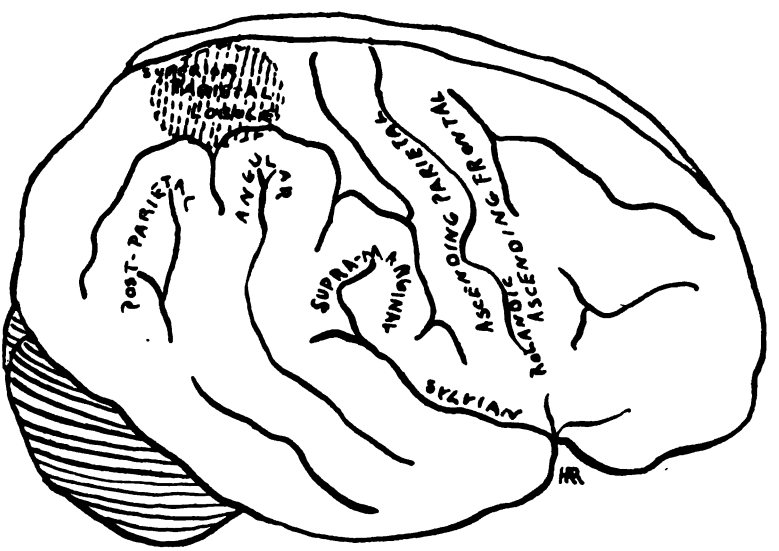

Fig. 130.—Case of E. C. The shaded area indicates the probable location of the vascular lesion producing the disturbances in sensibility.

Facial nerve: The motor function of the seventh nerve was normal. There was no objective disturbance in the sense of taste.

Glossopharyngeal, pneumogastric, spinal accessory, and hypoglossal nerves: These nerves were all normal.

Systemic Examination.—There were no particular abnormalities in the skin except the diffuse mottling of the skin mentioned before. There were no glandular disturbances. The cardiovascular system was normal, the heart was not enlarged, and

there were no murmurs. The blood-pressure was 130/90, the pulse 72, good quality, and the walls of the blood-vessels were not thickened. There were no changes in the respiratory, gastro-intestinal, genito-urinary, or skeletal systems.

The history as narrated by this patient clearly indicates repeated vascular accidents of sufficient extent and severity to produce extreme disturbances in spatial orientation. The basis for these vascular disturbances may clearly be found in her pregnancy and the resulting disturbed metabolic conditions. The residuum of these vascular disturbances is strictly limited to the cortical area responsible for the elaboration of the basic sensory components which are almost intact. The higher critical functions of the cortex are abolished and the functions of judgment and memory, with their companions of past similarities and dissimilarities, have been the major sufferers. The paucity of physical findings indicates a very limited area of disturbed function. The existence of the disturbed function of the superior parietal lobule and the absence of all other symptoms would seem to locate the lesion in this area of the brain.

CASE IV

A. N., aged sixteen. American. No occupation. Admitted to the Neurological Institute.

Present Illness.—*Chief Complaint.*—Convulsions with loss of consciousness.

Appearance of First Symptom.—May, 1921, and consisted in what we might call at this time a psychic equivalent, which will be described later.

Onset.—This was sudden.

Course.—The progress of the disease has been continuous, the attacks, as they are called, increasing in frequency and severity.

He had been perfectly well up to May, 1921, at which time, while riding his bicycle, he suddenly felt himself lifted off the seat. He dismounted and, after standing for a few moments, felt a throbbing pain beginning in the right side of the chest and extending upward into his head. The pain lasted for about

ten minutes and did not radiate into the arm or leg. He was fully conscious throughout the entire attack, and after the pain wore off he walked home, the pain disappearing entirely.

In June, 1921, while swimming in the tank at school during lunch hour, he was suddenly called upon to rescue one of his companions who was in imminent danger of drowning. While doing so he thinks that the other boy kicked him in the stomach, and a few minutes later, while standing by the railing of the pool, he experienced a second attack similar to the first, but of greater severity. This lasted about ten minutes and consisted chiefly in the same kind of pain outlined above. He had in addition to this a subjective sensation, as though his hand was jumping, but on looking at it he found that no actual movement was taking place in the hand. His right arm appeared semiflexed at the elbow, the fingers were stiff, and the entire arm felt as if it were held tensely by his muscles. In this attack he lost consciousness for a few minutes, the length of time he does not know exactly, but in any case it was for so brief a period that he was able to return to his classes at 1 o'clock feeling no immediate bad effects—no headache, nausea, or vomiting. There was no loss of sphincteric control.

In the interval between these two attacks there were minor seizures of a similar nature, beginning with the same pain and consisting in a pounding sensation, which at times extended into the right arm. These were very short in duration and during them he never lost consciousness. Often they were so slight that he could continue doing whatever he happened to be occupied in, although at first he was very apprehensive when they occurred and would stop and wait until they passed off.

About the middle of June, during the night, the patient had four severe convulsions, all of which occurred during his sleep, although some of them caused a brief period of wakefulness before the patient lapsed into unconsciousness. In one of these his brother saw him kicking around in bed, attempted to arouse him, but failed. He remembers nothing of these attacks, and states that there was a great tendency to fall asleep immediately after the attack was over. In none of them was there any in-

continence, nor did he ever bite his tongue. A general description of the attacks will suffice to describe each one. They all began with a pain on the right side in the lower part of the thorax which spreads upward to the head and outward to the shoulder, then down into the neck, arm, and fingers of the right hand. They were characterized by a throbbing pain with a rhythm which corresponded pretty well with the beating of his heart. This initial pain lasted for about five minutes and was usually a warning of the approach of a generalized attack. He occasionally had the pain as a warning and then the major attack failed to develop. When the convulsive seizure did follow, he noticed a forcible flexion of the fingers of his right hand so strong that at times the nails were driven into the palm of the hand and he was unable to extend his fingers. With the contraction in his fingers there was also a tendency to flex the forearm at the elbow, the arm was adducted, and the muscles held in a rigid spasm. On several occasions after the painful aura the right leg has gone into spasm instead of the right arm. With the severe attacks, following the convulsive movements of the right arm, there is a spread to the general body musculature, and a general convulsion follows, with loss of consciousness, cyanosis, and moaning.

These attacks have been more or less regular in their appearance, occurring about every three weeks. More frequently than the preceding, but with less regularity, there have been minor attacks in which he does not lose consciousness and in which the right hand, forearm and arm, or the right leg may go into spasm without any further spread in the manifestations of the attack.

During the first week in July the patient had two attacks while asleep, of which he knew nothing, but of which he was told by his parents. In August, 1921, again in the night, he had one severe attack. After this he felt no ill effects and was not inconvenienced in any way. During the period intervening between August and the middle of September the patient had only minor attacks which have been already described. On further questioning he describes the sensation in his fingers "as

if someone were holding the fifth finger tightly against the others."

About the middle of September, after considerable exertion in carrying a heavy object, he had a severe attack beginning exactly as before, radiating up into the head and into the right arm, in which the fingers of the right hand were drawn tightly together into the palm, the forearm was flexed, drawn up at the shoulder, and the whole arm adducted. Recognizing that an attack was imminent, he called to one of his companions, who, seeing his condition, instead of coming to his aid, ran away and left him. In an attempt to let himself slowly to the floor, he did not succeed, and fell. In this attack there were no jerking movements, the arm was held rigid and stiff, and he was entirely conscious of everything that was going on about him.

During September the patient noticed an increasing awkwardness in the use of his right hand which progressed to such an extent as to render him incapable of playing the piano.

During December he had one attack followed by headache, which has persisted off and on since then, and has been frontal in location. This is the first occurrence of headache noted in the history.

On January 17, 1922 he went home about 3 o'clock in the afternoon, took something to eat, and began to read. Suddenly he felt his head turning to the right as though someone were pushing it in that direction. He immediately lost consciousness and fell to the floor in a convulsion. During this attack he vomited. About one and a half hours after recovery he had a recurrence, in which his head again turned to the right, followed by a general convulsion and loss of consciousness. Since this attack he has had awkwardness and loss of the usual dexterity in the use of his right hand, and there is slight dragging in the right foot while walking. This attack was preceded by some dizziness, but not by the usual pain aura described before.

Past History.—It has been negative in all respects except for the following: He had mumps in childhood, an operation for right-sided mastoiditis in 1915. He had pneumonia in 1915, from which he made a perfect recovery. There has been no

history of any diplopia, failing vision, difficulty in hearing, or any other abnormality except as noted.

Family History.—His mother has had eight pregnancies, three of which resulted in accidental miscarriages. The father and mother are living and well. He has 1 brother who is in good health and 2 sisters who are well. There is no similar disease in any other members of the family.

Personal History.—The patient is right handed. He drinks tea and coffee moderately, but does not use alcohol or tobacco. He sleeps well and has a good appetite.

Physical examination showed the following facts:

Abnormal Attitudes and Deformities.—None noted or described.

Gait.—He is slightly unsteady, which is emphasized by efforts to walk on a straight line. The unsteadiness apparently results from an inability to use his right leg accurately. He is able to walk on his toes, on his heels, backward and sidewise, without any material increase in the unsteadiness.

Co-ordination.—Equilibratory: There is very slight swaying with his eyes open, and some increase in this upon closing the eyes. He stands well upon his left foot, but very poorly on his right.

Non-equilibratory: On the right the movement in the *finger-to-nose test* is unsteady, wavering, and presents oscillations which are increased upon removing the finger from the nose. The test is normal on the left side. The *finger-to-finger test* brings out the same wavering movements upon attempts to approximate the fingers. The *finger-to-thumb test* is done awkwardly, and there is a tendency for him to keep his eyes constantly on the right hand in order to perform the movements of the fingers. In the *toe-to-object-above-patient test* the same phenomena are observed, although less pronounced, and in the *heel-to-knee* and *along shin tests* there is the same condition of affairs. There is marked inability to produce rapid succession movements on the right side, and a marked loss in the check element on forced movements of the right arm.

Skilled Acts.—There is dyspraxia present in the right hand

and his handwriting shows marked awkwardness, irregularities, jerkings, and improper measuring in the direction and position of the letters.

Abnormal Involuntary Movements.—In addition to those contained in the history, there is a rather coarse tremor of the whole right upper extremity.

Reflexes (deep):

	Left.	Right.	
Pectoral	3	2	With spread to deltoid and biceps on the right side.
Biceps	3	2	
Triceps	3+	2	
Ulnar	2	2	
Wrist	2+	2	
Suprapatellar	2+	2	
Patellar	3+	2	
Hamstrings	3	2	
Patellar adductor	0	0	
Tibio-adductor direct	0	0	
Tibio-adductor crossed	0	0	
Achilles'	4	3	

Reflexes (superficial):

	Left.	Right.
Supra-umbilical	Present	Present
Suprapubic	±	0
Upper lateral abdominal	+	±
Lower lateral abdominal	+	0
Cremasteric	+	+
Plantar flexion	Normal	0
Babinski and modifications	0	0

Muscle Strength.—Power on the left side is normal. The right arm, forearm, hand, thigh, calf, and foot show some diminution in power. The upper extremity is more extensively involved than the lower.

Muscle Status.—There is no atrophy, hypertrophy, or any changes in muscle tone

Abnormal Associated Movements.—Not observed.

General Sensory.—Touch: Acuity is very slightly diminished over the entire right side except the face. This diminution can only be elicited by directly comparing the right and left sides. The localization of two points simultaneously applied to the

skin shows that the circles of Weber, to be recognized, require a diameter on the right side twice that on the left. This affects the hand, forearm, and arm. Touch localization is considerably disturbed, error in localization on the right being about twice that on the left. Pain: Normal on the face; elsewhere on the right side of the body a pin does not feel quite so sharp as on the left. The sensation of pin prick is retarded and somewhat more diffuse. Temperature changes are similar to those elicited under pain—diffusion of the area stimulated, retardation of the appreciation of the test-tube, and a slightly diminished acuity in recognizing changes in temperature. Vibratory sensibility is normal. Muscle tendon sensibility is very much diminished in the right thumb, slow circumduction not being appreciated. The loss in muscle tendon sensibility becomes progressively greater as the little finger is approached, extreme tension being necessary to cause an appreciation of movement in the little finger. Deep muscle sense is diminished in the wrist, somewhat diminished at the elbow and shoulder. In the lower extremity there is a marked disturbance in appreciation of movement in the toes which is especially marked in the great toe which requires an excursion of 3 to 4 cm. before movement is detected. Stereognosis: Ability to recognize a knife, fountain pen, watch, or coin is lost in the right hand, whereas they are instantly recognized in the left hand. There is acrognosis in the right arm, forearm, and hand.

Cranial Nerves.—Optic and Oculomotor Apparatus: Vision in both eyes is normal and the fields are normal. Fundi: There is a blurring of the disks on the upper and nasal side on both sides with a papilledema of 1 diopter in the right eye. Pupils are equal, 3½ mm. in diameter, round, regular, central in position; no hippus present. The reaction to light, direct and consensual, is normal. There is no Argyll-Robertson pupil. Position of the eyes is normal. There is no strabismus and no limitation of voluntary movement of the eyes. Nystagmus: There are slight oscillatory movements on extreme left lateral gaze. The palpebral fissures are normal.

Fifth nerve is normal.

Facial Nerve.—There is a slight awkwardness in movements of the right face especially marked about the angle of the mouth.

Eighth, ninth, tenth, eleventh, and *twelfth nerves* are all normal.

Systemic examination is normal.

LABORATORY REPORTS

Blood Examination:

Hemoglobin,	86 per cent.
Color index,	0.9
Red blood-cells,	4,780,000
White blood-cells,	5000
Polymorphonuclear leukocytes,	64
Lymphocytes,	34
Eosinophils,	2
Non-protein nitrogen,	28.2
Urea nitrogen,	13.2
Blood-sugar,	0.115
CO_2,	48.1 per cent.
Wassermann,	Negative

Spinal Fluid:

Appearance,	Perfectly clear
Tension,	Normal
Cells,	None
Globulin,	Negative
Fehling reaction,	Positive
Wassermann,	Negative

Urine:

Color,	Straw
Reaction,	Alkaline
Turbidity,	Slightly turbid
Specific gravity,	1.106
Albumin,	None
Sugar,	None
Indican,	Slight excess
Microscopic examination:	Triple phosphates
Phthalein excretion,	25 per cent. first hour
	10 per cent. second hour

Mosenthal nephritic test-diet was negative, the urea and chlorid excretion being normal.

x-Ray examination of the skull showed the calvarium to be even in outline and comparatively even in thickness; no definite evidence of increased intracranial pressure. Intracranial circulation was normal except for one diploic channel in the mid-

occipitoparietal region of the left side which was slightly widened. The sutures normally united. The frontal sinuses were absent. Ethmoid cells were not remarkable. The sphenoid cells were rather irregular in shape, not subdivided to such an extent as is usually seen. The mastoids were extensive on the left side. The sella was small and well rounded. The dorsum extended considerably above the level of the anterior clinoids and inclined slightly forward, giving a partially closed-in appearance to the sella.

Summary: No definite evidence of intracranial pathology.

The course following admission showed no particular abnormalities. There was some headache, dizziness, and occasional warning of attacks which did not materialize. On one occasion he was nauseated and vomited after a severe headache.

The diagnosis was a neoplasm, probably an endothelioma, situated on the surface of the brain in the left superior parietal lobule. Operative interference was advised and he was transferred to the Surgical Service of Dr. Charles A. Elsberg.

On January 31, 1922 examination showed approximately the same signs and symptoms as enumerated above except that there was an increase in the hyperreflexia on the right side, with the production of a pathologic inexhaustible ankle-clonus.

He was operated upon January 31st, the operation consisting in a left osteoplastic flap. The bony tissue was found to be fairly thick and quite vascular. The dura was very vascular, not discolored; the tension was markedly increased. There were no focal irregularities or changes in contour observed. Puncture of the ventricle was attempted, but was not successful.

Situated in the superior parietal lobule there was discovered a tumor about 5 x 6 x 3 cm., which was adherent to the dura over a small area about 3 cm. from the midline. The tumor began at the Rolandic fissure and extended backward into the superior parietal lobule over an area about 6 cm. in diameter. The cerebral convolutions about the tumor appeared normal in color and consistency. The tumor was well encapsulated about most of its periphery, but was not clearly differentiated from the cortex in the deeper areas and there was some destruction of

the brain tissue as the tumor was removed. The tumor was not particularly vascular. On account of its relationship to the large veins in the Rolandic fissure there was considerable hemorrhage after its removal, and the patient went into severe shock, for which appropriate treatment was given at the time with a rapid improvement in his general condition. The tumor was entirely removed in pieces and the operative defect was closed in the usual manner. He rallied well from the operation and has shown a continuous progressive improvement ever since.

Pathologic Report of the Tumor by Dr. Casamajor

Diagnosis.—Angiosarcoma. The tumor consists of many small blood-vessels with cells arranged rather irregularly about them. Some of these cells are small thin spindles, while others are irregular, rounded, containing large rounded or oval, rather faintly staining nuclei. In some of these nuclei vacuoles appear. These latter cells tend to gather together in irregular rounded masses. Both types of cells are irregularly arranged around blood-vessels; there is much free blood in the tissues.

On February 8th the papilledema had practically disappeared.

Examination on February 4th showed that there was some improvement in the deep muscle sense in the right hand, improvement being more marked in the preaxial than in the postaxial portions of the hand. He had regained his ability to recognize a knife, safety-pin, and realized that a spoon had a handle and a hollow bowl, but was not able to synthesize these fragments of information into ability to name the object. The reflexes were as before, the ankle-clonus was still inexhaustible. The general condition was very good.

On February 14th examination showed continued improvement in his ability to recognize movement and objects. There was still some ataxia present which was especially marked in the large joints of the right arm and leg.

Following the operation there was no material motor weakness in the right upper or lower extremity except that immediately following the operation there was a series of rapidly repeated convulsive seizures, four in a period of half an hour, in

which the right side was affected with marked convulsive movements of the right hand and there was a paralysis for one and a half hours in the right hand.

Physical examination made on March 8, 1922 showed the following:

Interval History.—The patient states that he has improved in every way. He has had no convulsions, no headache, and the only abnormal sensation of which he complains is a feeling of tension between the thumb and index-finger of the right hand. He has resumed his piano playing and can do it very well with the right hand, though not so well as with the left.

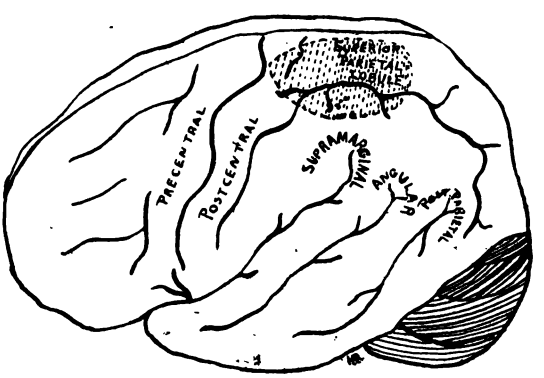

Fig. 131.—Lateral aspect of the left cerebral hemisphere indicating the position of the neoplasm.

Physical Examination.—*Abnormal Attitudes and Deformities.*—There is a scar of recent osteoplastic flap operation in the left parietal region. At the lower anterior angle of the left parietal bone there can be palpated a small bony defect. There is no bulging and the bone is solidly in place.

Gait.—There is some slight unsteadiness in turning both to the right and left; otherwise it is normal.

Co-ordination.—Equilibratory.—Normal both with the eyes open and closed. Standing on the right foot is not quite so well done as standing on the left foot.

Non-equilibratory: In the *finger-to-nose test* there is some oscillation toward the end of the act, but not on maintaining the

finger on the tip of the nose. The same is present in the *finger-to-finger test*. The *heel-to-knee test* is well done on both sides, but the *heel along shin test* on the right side shows some wavering. The *toe-to-object-above-patient test* is normal on both sides.

Fig. 132.—The shaggy appearance of the under surface of the tumor which showed rather intimate relationship to the underlying brain tissue.

Dysmetria.—There is some loss of the check element and overreaching in movements performed with the right hand.

Adiadokokinesis is present in rapid succession movements of the right hand.

Skilled Acts.—There is an awkwardness on attempting to snap the fingers, although this can be done fairly well with the

right hand, and also upon approximating the right thumb to the fingers of the right hand. The speech is normal. The handwriting is slightly better than formerly.

Reflexes:

	Left.	Right.	
Jaw	2	2	
Pectoral	2+	3	
Biceps	2+	3+	
Triceps	2+	3+	
Radial	2	3+	
Ulnar	2	3+	On the right side there is an active spread from the ulnar and radial reflexes to the biceps and triceps.
Suprapatellar	0	1+	
Patellar	2+	3+	
Achilles'	3+	5	
Periosteal uncrossed	0	+	
Periosteal crossed	0 L.-R.	0 R.-L.	
Ciliospinal	±	±	
Abdominals	+	0	
Cremasteric	+	+	
Plantar flexion	+	0	
Babinski	0	+	
Chaddock	0	+	
Oppenheim	Plantar	Plantar	
Gordon	0	0	
Schaefer	0	0	
Fanning	0	+	

Muscle Strength.—On the right side there is a slight symmetric weakness in all movements, more marked in the upper than in the lower extremity. Efforts at forced movements in the right hand cause a clonus at the wrist.

Muscle Status.—There is no atrophy or any change in contour; tone is apparently normal.

Abnormal Associated Movements.—The pronation sign of Strümpell is positive in the right upper extremity; negative in the left arm.

The radialis sign of Strümpell shows a definite increase in the flip of the right wrist dorsally on closing the fingers.

The thumb sign of Klippel-Weil shows more movement toward flexion of the distal phalanx of the thumb when the

clenched fist is forcibly opened on the right side than on the left side.

There is no Hoffmann sign present.

The sign of Neri produces a slight flexion in the right leg upon flexing the extended leg on the abdomen.

There is some elevation of both legs in the trunk-thigh sign of Babinski, but the movement is a little more marked in the

Fig. 133.—The microscopic appearance of the tumor. The rich vascularity of the neoplasm is very evident. The character of the tumor is indicated by the bundles and groups of spindle-cells which often seem to radiate from bloodvessels. In other areas large vesicular nuclei appear embedded in a syncytium. There are a number of these cells the nuclei of which contain vacuoles.

right leg. Modification of the trunk-thigh sign of Babinski, with the legs hanging over the table, is positive on the right, negative on the left side.

The coughing sign of Huntington is present on the right, not on the left side.

The complementary opposition sign of Grasset and Gaussel and of Hoover is present, greater downward pressure being excited by the left leg in elevating the right than vice versa.

The tibialis sign of Strümpell cannot be elicited.

The sign of Marie-Foix is not present.

Sensory Examination.—Touch is normal everywhere except for a little hypesthesia on the dorsum of the right thumb and the right index-finger. Localization: There is about the same error in the forearms on both sides, but the error in the right arm and shoulder is about twice that in the left arm and shoulder.

Muscle tendon sense is very much disturbed in the right hand, fingers, wrist, elbow, and shoulder, but particularly so in the fingers. The same is true of the right foot, but to a much less degree and limited to the toe-joints.

Stereognosis: He can now recognize a knife, safety-pin, coin (but he misses the denomination of the coin), and a fountain pen. On the right hand he cannot distinguish between a square and a round object rolled over the fingers.

Cranial Nerves.—First nerve is normal.

Optic and Oculomotor Apparatus.—Vision is normal. Ophthalmoscopic examination shows evidence of a recent papilledema, the right disk is indistinct and blurred except below and laterally; elsewhere there are some radial markings running over the edge of the disk; the veins are somewhat tortuous. In the left eye the outline is slightly less distinct than in the right eye. There are no hemorrhages. Pupils: The right is 2½ mm., round, regular, and central. The left is 3 mm. There is marked hippus present. The pupillary reaction to light, direct and consensual, and on convergence is normal in both eyes. The palpebral fissures are normal. There is no strabismus. The conjugated eye movements are normal. Nystagmus is not present.

Fifth, seventh, eighth, ninth, tenth, eleventh, and *twelfth nerves* are normal.

The *systemic examination* is normal.

The condition presented by A. N. is considerably simpler than the preceding case in some respects, while in others it presents features the exact evaluation of which is but at best speculative.

In considering the case the facts lead one to the diagnosis of an organic lesion in the brain, affecting the superior parietal

lobule and manifesting its presence primarily, so far as the examination goes, by disturbances in the cortical association, correlation and synthesis of the primary qualities of sensation as received by the post-Rolandic cortex and transmitted to the superior parietal lobule for elaboration. In regard to the history the condition is mainly characterized by evidences of cortical irritation manifesting themselves in two types of seizures, one abortive and resulting only in a pain aura and spasmodic contractions of the right arm and forearm; the other by major attacks which develop out of the minor attacks and proceed to a general convulsive seizure, loss of consciousness, and the usual postconvulsive habitus. The history and physical examination present the evidence of an expanding neoplasm situated on the left side of the brain, affecting primarily the secondary sensory association centers and secondarily the motor cortex. The disturbances present an adiadokokinesis, a dysmetria, and an ataxia which are sensory in character and largely dependent upon faulty appreciation of the position of the muscles in space and the consequent disturbance in the motor pattern as manifested in attempts to produce rapid succession movements and voluntary acts. The reflexes are indicative of pressure upon the pyramidal system passing to the right side of the body, with a general increase of the reaction of the right-side reflexes, loss of the superficial reflexes, and the presence of some of the abnormal tendon and cutaneous reflexes on the right side. The failure of the great toe on the right side to go into plantar flexion or dorsiflexion upon stimulation of the sole of the foot is indicative of the fact that in the development of the Babinski there is a period, so to speak, of equilibrium when neither dorsi- or plantar flexion results from stimulation of the sole of the foot. The changes in muscle strength indicate a partial interference with the function of the pyramidal tract going to the right side. The sensory disturbances indicate the results of pressure on the post-Rolandic convolution producing a very slight diminution in the cortical appreciation of touch, pain, and temperature. The cortical synthesization of touch, pressure, muscle tendon, the effects of contour, form, size, and weight are completely

eradicated by the involvement by the tumor mass of the functions which we know reside in the superior parietal lobule. The fact that vibratory sense has remained unchanged would lead one to the conclusion that the representation of vibratory sensibility in the cerebral hemisphere largely resides in the subcortical centers, namely, the thalamus. It is a matter of common knowledge that vibratory stimuli are far more colored by the affective type of sensibility than by the discriminative. The instinctive reaction of children to vibratory stimuli, shown by the withdrawal of the part from the tuning-fork, is repeatedly seen, and the same phenomenon in adult patients where the intellectual grade is not very high. The unpleasant character, for example, of the dentist's drill, even in the absence of pain, and the very unpleasant sensations produced by the deep tones in a whistle or in an organ, are matters of common experience. Discriminative recognition of rates of vibration even very widely separated is quite difficult, and the chief reaction subjectively obtained is that the deep resonant vibrations are distinctly more unpleasant than the more rapid and less ample vibrations. These facts seem to indicate that the cortical representation of the vibratory sense is very limited, and its main end station would then seem to be in the thalamic centers. In none of the cases of pure cortical anesthesia, so far as has been demonstrated at operation in the past six months, has there been any material disturbance in the vibratory sense, and it seems fair to conclude that the major representation of the vibratory sensibility is in the thalamus.

The disturbance in pain and temperature sense consists in a moderate reduction in the acuity of perception to hot and cold and of the sharpness of the pin prick. The hurt element, which is believed to be largely thalamic in origin, is retained; but the cortical contribution in recognition of pain—that is, its location, its sharpness, and the promptness with which it is appreciated—are diminished to a slight extent. It seems quite self-evident that there must be some discriminative elements in the appreciation of pain and temperature, and in the disturbance as shown

here there is a fair indication as to what elements of pain and temperature sensibility reside in the cerebral cortex.

In considering the disturbances of sensibility it is necessary to study the type of aura in this case. This consisted of a pain originating in the lower part of the thorax on the right side, and spreading upward to the head and outward to the arm. It is difficult to conceive of any explanation for painful auras in these conditions, but it may perhaps be possible to consider that the factor in this case has been some vascular disturbance in the tumor making itself felt first in the area represented by the middle part of the post-Rolandic convolution upon which the cephalic border of the tumor impinged, and then spreading downward along the post-Rolandic convolution and manifesting itself as a referred pain with its distribution first in the thorax, then in the arm, and finally in the head. The fact that the aura consists chiefly in pain may be explained by an excitation of the corticothalamic fibers passing from the post-Rolandic area to the thalamus, in which case the cortical arrangement would present the pattern of the disturbance, whereas the thalamus contributes the affective elaboration, namely, pain. This second view is more appealing than the first, for it is common knowledge that under local anesthesia the cortex may be incised without the production of any pain, and we must postulate some disordered function indirectly stimulating the thalamus and thus evoking the intrinsic function of this portion of the brain. The appearance of the Jacksonian symptoms in the hand may be explained on a rather theoretic basis. It is known that the main function of the superior parietal lobule is to supply the discriminative forms of sensibility which reach their acme in the hands and fingers. The connections of this area with the region providing for the production of voluntary movement are, in all probability, more intimate and extensive for the hand than for any other part of the body, and it seems quite conceivable that an excitation originating in the superior parietal lobule might manifest itself by motor disturbances in the area most richly connected with this part of the brain, namely, the lower third of the precentral convolution. It is known that the

sensory apparatus is developed for the purpose of producing motor reactions, and it may be that on account of this fact and the intimate connection between the two areas involved that abnormal impulses originating within this sensory cortex may result in these evident motor disturbances.

The pathology coincides with remarkable exactness to the anatomic delimitations of the functions of the superior parietal lobule.

ANESTHESIA DUE TO LESIONS IN THE SUPERIOR PARIETAL LOBULE

The essential character of the activity of the cerebral cortex in the function of sensibility is the application of memory to the critical appreciation of sensory stimuli. Memory is the retained concept of some preceding group of stimuli. The cortical function is never a simple one; never confined to a single type of sensation or of special sense. It is always complex, an integration of related sensory or motor effects, a synthesis of former stimuli which may or may not have led to a definite mental concept, but which has always led to a more or less permanent mnemonic impression. The permanency of the impression depends either upon its profundity or upon its repetition. A single occurrence may be of such importance, either in regard to itself or in relation to its attendant circumstances, as to produce a lasting impression. Many single happenings produce results which last as long as life itself and are capable of being recalled at will or fortuitously by the recurrence of similar attendant, antecedent, or resultant phenomena. Other stimuli of less consequence or amplification impress consciousness sufficiently to rise into the focus of attention only by a longer or shorter period of repetition in which the synaptic junctions afford an easier and easier path of conduction and thus become more and more fixed and thus capable of reproduction. The retention of past impressions and their comparison with contemporaneous stimuli afford the basis for judgments as to their relations toward one another both in regard to their similarity or dissimilarity. At the same time there is set into motion a

train of memory pictures which recall the consequences of former sensory impressions and their associated processes. Such judgments are then compared, the results of action based upon similar judgments reviewed in regard to their consequences, and the conclusion is then represented by the individual's motor or psychic reaction. This process may be viewed as the faculty of reason, and as reason dictates so will the individual's behavior be regulated. A large contribution to this process is supplied by what are called the affective sensibilities, that is, the pleasure-pain components in the sensory life of the individual. These constituents figure very largely in the instinctive reactions, attraction or repulsion being almost the foundation for the behavior which safeguards the propagation of the species and the perpetuation of the individual. These reactions can be found operative far back in the phyletic scale, antedating by many developmental eras the appearance of the cerebral cortex, and therefore their seat must be sought in primitive structures which are still extensively functioning in the human individual. Such a structure is provided in the optic thalamus, and this morphologic unit is viewed as being the end-station in consciousness of the types of sensibility most closely associated with the instinctive reactions in the preservation of the sense of well-being, that is, pain, temperature, and probably vibration. These three types of sensibility unelaborated by the discriminative and comparative functions which are evolved from them by the cerebral cortex reach their final end-stations in the nuclei of the optic thalamus. Formerly the optic thalamus provided functional end-stations for all the various crude streams of somesthetic sensibility which we have followed coursing upward along the various tracts in the spinal cord, but as the organization of the individual became more complex and as the behavioral reactions increased in richness and elaboration, this structure became inadequate to the increasing demands made upon it by the expanding reactions of the individual. As a consequence the cerebral cortex appeared and provided ample areas for extension and consolidation of these interreactions, and a stepping upward of these functions took place, affecting all

except the pain, temperature, and vibratory sensibilities which retained the former end-stations in the thalamus. The particular area which supplied this new field for expansion has become, in man, the parietal lobe, and in the cephalic portion of the parietal lobe, in the ascending parietal convolution, we find the new area for the reception of the unclassified, uncatalogued, crude sensibilities of touch, pressure, muscle tendon, and ligamentous sensibilities.

There are, then, coursing upward from the spinal cord to the thalamus and the cerebral cortex the following crude and unelaborated streams of contribution to somesthetic consciousness: pain, temperature, vibration, touch, pressure, and tension in regard to muscles, tendons, ligaments, cartilages, bones, and the periosteum. In the spinal cord these streams exist as simple, unrelated contributions to the sensorium, and injury to any of them at any point along their course will result in damage to the particular constituent or constituents affected and also in an impoverishment of the elaborations made possible by the synthesization and correlation of these simple building-blocks in the cortex. The essential character of lesions in this parietal lobe caudal to the ascending parietal convolution is that no one of the aforementioned simple streams of sensibility is affected, but only the ability to correlate and elaborate the less organized stimuli into the complex and intricate concepts of concrete objects and images. Lesions of the parietal lobe behind the postparietal gyrus present the tactile, pressure, pain, temperature, and vibratory sensibilities to all intents and purposes unaffected, but the appreciation of the degree of sharpness or the delicate differentiation between intermediate degrees of temperature, the determination of the extent of movement in the joints, the tensions upon muscles, tendons, and ligaments, the exact localization of stimuli upon the surface of the body, the differentiation between the simultaneous stimulation of two points upon the skin, and finally the ability to recognize objects and to apply the proper names to them without the use of the special senses are profoundly affected, the exact extent dependent upon the degree of cortical damage.

Analysis of the cortical functions of sensibility shows that the lesion has removed the basis for judgment and ideas. The memory or retention ability of the mind in the particular sphere of somesthetic sensibility has been destroyed or suspended. This deprives the individual of the vast stores of knowledge which all the preceding years of his life have built up out of the multitudinous contacts of his life and experience. Each stimulus arises into consciousness as an isolated, unrelated phenomenon. It can no longer be compared with preceding stimuli, and hence cannot be found to be similar or dissimilar in character to those which have preceded it.

It will be worth while to examine each type of sensibility in order to obtain a clear picture of what the results of such psychic impoverishment has done for the individual. The stimuli of pain can still be recognized, but what is the difference, the quality of sharpness is gone and what remains is a sensation of discomfort and distress. The individual can no longer discern between degrees of sharpness, only between major differences in pain appreciation. Pain has lost its cortical component and only appears as distress, a disturbance in the sense of well being, a purely thalamic reaction. All the memory of former painful and sharp experiences has been obliterated and the individual can no longer compare the present stimulus with foregoing sensations, and he merely says that it hurts. If asked to determine between the degrees of sharpness as presented by two points differing in pointedness, he can simply say that one hurts more if two points are simultaneously applied. If an appreciable interval elapses he cannot state which hurt more. The sensation received from the affected area is also perverted, it often becomes burning or scratching in character, and seems as if applied to a considerable surface, that is, the acute normal power of localization is lost. The sensibility to heat is also affected in a similar manner, the basis for comparison is gone, and each stimulus is judged on its own merits. The disagreeable thalamic element is no longer controlled by the critical discriminative function of the cerebral cortex. All sources of painful stimuli have become similar, the very different impressions

of pain when produced by pressure, pin prick, temperature, overextension of joints then become merged into a vague, ill-defined sensation of discomfort.

Muscle tendon sensibility is profoundly affected by lesions in the parietal lobe. If this sensibility is analyzed, it is evident that the conception of the amount of tension exercised by varying postures upon the muscles, tendons, ligaments, and bones is distinctly a comparative one. The result of a synthesization of such impressions and their comparison with preceding postures supplies us with our ideas as to the position of the limbs, fingers, and toes in space. If the memory concepts of such foregoing stimuli be erased, the individual is at once deprived of all the criteria by which he can judge as to this spatial orientation, and as a result he loses all ability to tell in what position his limbs have been placed or have voluntarily moved themselves. The knowledge that his toe has been pressed backward depends upon his memory pictures of the sensations produced by such a movement in the past, proved either by vision or by digital examination. If these be impossible and the comparative functions lost, the inrushing stream of impulses lose all their significance, he no longer knows whether his toe is moved up or down, or to what extent such a movement has taken place. This impoverishment manifests itself more and more extensively the smaller the joint affected and the finer the movement produced. The recognition of movement depends almost completely upon comparative mnemonic impressions, and lesions in the parietal lobe destroying these reservoirs of past experience completely deprive the individual of his sense of spatial orientation.

The ability to localize stimulating impressions on the surface of the body depends directly upon the retention of past memory impressions of similar mechanisms. The individual's knowledge of his superficial area has been developed by years of contact with environmental impressions. Stimuli from any given area have been received thousands and thousands of times, and the investigation of the source of such stimuli by the eyes or the fingers has resulted in the development of a very definite topographic sense in the cortex. The process of the development of

such a sense is evident in the reactions obtained in children of different degrees of cortical differentiation. The youngest betray no effort at real localization, the only response is a thalamic one, the withdrawal of the entire part from the stimulating medium. Only after repeated stimuli have been received and the position of the cause of the sensation ascertained by vision or investigation does the localizing sense develop. The loss of the ability to recall such former stimuli and their position either completely or incompletely, according to the severity of the disturbance, destroys the faculty of sensory localization. So in an even greater degree the ability to judge of the distance separating two simultaneously stimulating points is affected by cortical lesions of this type. This is, of course, evidently a matter of comparison and judgment, and as the elemental concepts on which such a judgment can be based are destroyed, it is obvious that the individual can only roughly estimate the distance separating two points simultaneously applied to the surface of the body.

The disturbance of the vibratory sense seems minimal in these cases. As discussed in connection with the case A. N., the chief end-station of the vibratory function seems to be in the thalamus, both on account of its effective coloring and upon the minimal discriminative power of the cortex in regard to vibratory stimuli. Lesions of the cortex affect vibratory sensibility little if any, and it seems justifiable to believe that its entrance into the higher level of the cortex is only to a very slight extent.

The finer power to distinguish between varying kinds and qualities of tactile stimuli seems to be essentially a cortical activity. In all of the illustrative cases the crude sensation of contact seemed well maintained. In no case was there any material interference with the appreciation of cotton-wool throughout the entire cutaneous surface. In particular, each delicate touch of a wisp of cotton was keenly appreciated over the area which was deprived of its cortical elaborative expansion in consciousness. If, however, various kinds of stimuli were used, there was found to be a profound disturbance in the appreciation of the substance producing the sensation. The individual was unable to distinguish between sensations produced by cotton, silk,

velvet, rubber, and many other equally or more dissimilar materials. This also indicates the loss of the retentive memorizing faculty in registering cutaneous stimuli. Normal individuals learn to make these discriminations through long series of the application of trials with success and failure attending them. Each success or failure has served to crystallize the memory concepts of the results of various kinds of stimuli, and the destruction of this elaborately critical and discriminative function in the parietal cortex results in the loss of the penumbra which normally surrounds the cortical impressions of stimulating media. The patient knows he is being touched, but he no longer possesses the elaborative mechanism by which he can distinguish between or identify various kinds of stimuli.

The highest level of cortical function in this great somesthetic area combines all the foregoing types of sensation, both crude and elaborated, together with the ability to connect the object with its name, that is, the exclusively cortical function of the recognition of an object by means of its form, size, weight, contour, surface impressions and consistency, and its identification with a name without the use of any of the special senses, namely, stereognosis. This is the highest development in somesthetic synthesization. In addition, there is brought into play here the interfunction of other areas, namely, those of the special senses with the nominating area. The identification of objects by their shape, size, consistency, weight, contour, etc., has been further amplified through all the years of past experience by the sense of sight, hearing, and, to a less extent, smell. As a result of such a synthesization we are able to form concrete images of different objects and give to each and every one its correct and proper name. This brings into action remote areas in the building up of this complicated concept and the various association tracts seem to link together the visual, auditory, olfactory, and frontal areas with the parietal lobe as the vortex of these streams of association fibers. The complex character of this association is clearly exemplified in the case of A. N. Before the operation this patient was absolutely unable to identify or name objects by the sense of touch. He had com-

pletely lost his stereognostic sense. After the operation we observed a slow reintegration of this function. At first he was able to recognize only gross differences in shape and form. As the cortex resumed its activity he was able to make finer and finer correlations and comparisons until, shortly before his discharge, he was able to say that an object placed in his hand was thin, that it had a hollowed out, expanded end to which was attached a somewhat lengthened narrow prolongation, and yet he was unable to recognize such an article when described as a spoon. This nominating faculty was the last to return, and he is now able to recognize without the aid of the special senses any object placed in his hand.

These, then, are the intimate functions of the parietal lobe so far as our crude methods of examination are able to elicit them. What refinements still remain undiscovered in the cortex will be disclosed only by further study and investigation, but we can state with security that the basic underlying faculty is that of retaining past impressions as a basis for comparison as to similarity or dissimilarity, namely, memory. Such undisturbed correlations and synthesizations are necessary for us to be able to elaborate our higher cortical functions, and disturbance of them leaves consciousness mutilated and unable to furnish its full quota to the end of all cortical activity—individual behavior.

CLINIC OF DR. BRET RATNER

DEPARTMENT OF CHILDREN, VANDERBILT CLINIC

CERTAIN ASPECTS OF ECZEMA AND ASTHMA IN INFANCY AND CHILDHOOD FROM THE STANDPOINT OF ALLERGY

THE knowledge of protein hypersensitiveness enables us to far better understand and treat patients suffering from eczema and asthma than we have heretofore been able to do. A number of cases will be selected for this clinic from a large group in an endeavor to bring out some of the salient features that underlie this hypersensitiveness in infants and children, and its treatment.

GROUP I. SHOWING THE RELATIONSHIP BETWEEN ECZEMA AND ASTHMA

Case I.—F. K., a male child twenty-three months old, was first seen by us at the age of four months, suffering from a moderate eczematous condition of the face. The family history for protein sensitization was negative except for a maternal uncle, who suffered from asthma. A simple ointment was prescribed and the mother was asked to return with the child for further study, but failed to do so for a period of nine months, when, at the age of thirteen months, the child was admitted to the New York Nursery and Child's Hospital suffering from a severe attack of asthma.

Upon investigation into the history the mother stated that in the preceding four months the child had had about seven attacks of what was then diagnosed acute bronchitis. However, the mother definitely stated that the child had no pyrexia during these attacks. The eczema that the child had at the

age of four months persisted through this period, with definite clearing up at times.

The child was entirely breast fed when he first came to our clinic, and at the time of admission to the hospital was still receiving breast feedings, but, in addition, also cow's milk and other foods. It was learned that the child had taken all his foods well with the exception of egg. When a small amount of soft-boiled egg was first offered him at the age of nine months he promptly vomited it. Subsequent attempts to offer the child egg were always met with absolute refusal, and after three such efforts—according to the mother's statement—the child never received any egg. However, further inquiry showed that the child had received cakes and other egg-containing foods.

The physical examination at the time of admission presented the typical signs of asthma and also a moderate eczema of the face.

Cutaneous skin tests were done by the scratch method with all the foods the child had taken. The reactions to egg-white and ovomucoid were strongly positive.

After the child was discharged from the hospital, cleared of his asthma, the mother returned regularly with him to the clinic for subcutaneous desensitizing injections of egg-white solution. The mother was duly impressed with the importance of rigidly eliminating all forms of egg-containing foods from the child's dietary. For a period of two months the child was injected—the eczema was entirely cleared and there had been no recurrence of the asthma. However, at the age of fifteen and a half months—that is, two and a half months after the last attack of asthma—the child came to the clinic presenting the following conditions: The eczema of the face had returned; there were several urticarial wheals scattered over the body, and the lungs contained numerous sibilant and sonorous râles. The mother denied having given the child any form of egg, but upon insistent questioning finally suggested that the previous day they had visited the grandmother, who might have given the child a piece of cake. It was soon after leaving the grandmother's home that the child developed the dry cough which

was probably the beginning of the attack. The fact that the child had eaten a piece of freshly baked cake was confirmed the following week.

The child returned regularly to the clinic without any further attacks of asthma or return of eczema until three months later, when for a period of three weeks the child always presented asthmatic râles, with a dry, non-productive cough. At these three visits the mother regularly denied having given the child any form of egg-containing food, but after persistent quizzing about any new foods she innocently stated that the child had been getting noodles for the past four weeks. Again she was advised to absolutely eliminate all egg-containing foods, and for the past months the child has been free from all symptoms and is still receiving injections of egg-white. These injections are all below the child's threshold and have caused no local or general reaction. We had started with 0.05 c.c. of a 1 : 50,000 dilution and our last injection was 0.4 c.c. of 1 : 5000 dilution of egg-white.

Summary of Case I.—An infant who suffered from eczema at the age of four months returned to the hospital at the age of thirteen months suffering from asthma. A history of recurrent attacks of so-called bronchitis—without pyrexia—was obtained, since the child had been taking egg-containing foods. A history of intolerance to egg was also shown and skin tests revealed sensitization to egg-white. The child is twenty-three months old at the present time, and during the past ten months of observation has had several attacks of asthma and a return of eczema which we have shown to be due to the ingestion of cakes and noodles. Since we have been able to eliminate all the offending foods the child has been perfectly normal in every respect, and he is at the present time receiving subcutaneous injections of egg-white in a dilution of 1 : 5000.

Discussion of Case I.—Unfortunately we were unable to do any skin tests when the child first came to us with the eczematous condition of the face, but we feel fairly certain in the light of subsequent findings that the original eczema was due to egg-white sensitivity, even though the child was breast fed.

O'Keefe[1] and Shannon[2] have suggested the very interesting possibility that foreign proteins may be transmitted through the mother's milk.

We have been able to show that the attacks of asthma were due to the ingestion of egg-white. With these attacks we have always had a return of eczema and on one occasion urticaria. The relationship between the asthma and eczema in this case is, therefore, evident, and this relationship has been emphasized by practically all the recent workers in this field.

The question of food dislike is one of more than passing interest, and individuals having these dislikes may be divided into two groups. In the one are those who dislike certain foods for some psychical reasons, namely, because the food has been poorly prepared, or the individual has eaten it to excess, or in the case of the typically spoiled child that refuses all food. In the second group may be placed those who have a true intolerance to certain foods, which the above case well illustrates. One must have a true respect for an infant's food intolerance of this type, as it usually suggests definitely a hypersensitiveness which may be the forerunner of a case of eczema, asthma, or urticaria. The particular protein, which in this case was egg-white, acted as a direct poison, and the vomiting was a natural attempt to prevent the ingestion of this toxic product. However, certain proteins are present in many food preparations and it is of paramount importance, in diagnosing and treating these cases, to understand thoroughly that the particular protein the patient is sensitive to may be ingested in some disguised form. For example, with egg-white it is well to know that all cakes, sweet crackers, certain candies, icings, charlotte russe, zwieback, noodles, some breads, French ice-cream, Italian ice-cream, certain gravies, puddings, etc., contain egg, and only after these are eliminated will an intractable case of eczema or asthma, due to egg-white, be free from symptoms, as was brought out in the above case. Once all the offending protein is kept away, then only can desensitization either by giving minute doses by mouth or by subcutaneous injection be attempted.

Many physicians still labor under the impression that very young infants do not suffer from asthma, and a diagnosis of bronchitis or pneumonia is usually made. Recurrent attacks of hyperpnea or dyspnea without a rise in temperature and with lungs containing sibilant and sonorous râles which gradually clear up in twenty-four to seventy-two hours should be looked upon as asthma, no matter how young the infant; and the cessation of râles after the injection of adrenalin or atropin will prove the diagnosis.

Those who have worked on asthma in adults have found fewer reactions to foods than those of us who work with children exclusively, and their conclusions have been that food hypersensitiveness is naturally overcome. It is true that desensitization may be brought about in untreated cases by the continued natural ingestion of small amounts of the offending protein, but it is far better that all cases be treated as early as possible, and thus prevent the retardation of the normal development of the child and the severe suffering that these diseases create. If Case I had been brought back regularly after the age of four months he would probably have been cured long before he was twenty months old—as subsequent cases will illustrate—and he might never have developed asthma. Had he not returned at thirteen months he might have gone on as the following case did for ten years, a severe sufferer from asthma.

Case II.—F. R. This boy, who is eleven years of age, was referred to us October, 1920 suffering from asthma. His past history was very indefinite except for the fact that the child had eczema in his early infancy, and as long as the mother could remember has been a continual sufferer from chronic coryza and asthma. The patient had occasional attacks of urticaria. At the age of five years his tonsils and adenoids were removed, but the asthma continued. The mother had taken the patient from clinic to clinic to seek relief, and two years before coming to us he had been tested and was found to be

sensitive to certain proteins, but no beneficial results were obtained from the treatment then instituted.

At the time the child first came to us he was found to be 10 per cent. underweight, anemic, with flattened chest, round shouldered, and of poor posture. His lungs were filled with asthmatic râles. The von Pirquet test was negative and the *x*-ray of the chest showed a marked hilus fibrosis, suggestive of chronic bronchitis.

As long as could be remembered the child always had an aversion for eggs and milk. An incident in the past history that arouses some interest (which the mother states she remembers as clearly as of today) is that the father gave the child a small amount of an egg-nog—made of milk, egg, and whisky —when he was two days old.

Skin tests were made with practically all the proteins and a positive reaction was obtained to egg-white, milk, and lactalbumin; egg-yolk, casein, and ovomucoid were negative.

Our first step in the treatment was to eliminate every form of egg and milk in the boy's diet, and with that end in view to the mother was explained every possible form of food that egg and milk might be present in. At first it seemed a very difficult task to give any form of diet to a child of this age without these articles of food, but after considerable detailed explanation with planning out of menus the mother finally gave excellent co-operation. For example, the child could have all vegetables, meats, fishes, fruits, nuts, olive oil, and cereals. The beverages allowed were weak tea and weak cocoa made without milk. Subcutaneous injections of egg-white and lactalbumin were commenced, starting with a dilution weaker than the one he reacted to, simultaneously with the elimination of these foods from the diet. During the first month and a half of treatment the child remained comparatively free from attacks, but his chest did present asthmatic râles at the various visits. Investigation into his diet showed that milk was used in the preparation of the bread that was bought. The mother then started to bake her own bread, but still after three more weeks of observation occasional rhonci were heard, and at this time it was

learned that since the elimination of milk the child ate large amounts of butter. This was substituted by oleomargarine (the variety in which milk was not used in manufacture). On two other occasions in the following month asthmatic râles were again heard, in one instance after indulging in ginger snaps (egg?), and in the other after partaking of chicken stuffing which contained milk and butter. No real attack of asthma was precipitated by these indiscretions, but asthmatic wheezes and a cough were produced. After these dietary considerations were finally overcome the child began to show marked improvement. He gained in weight, and for the first time in years had bright eyes and good color. The treatment which was first begun October, 1920 necessitated the child's coming to the clinic regularly three times a week throughout the severest winter months, and on the severest days the boy remained free from all catarrhal symptoms, and even played in the snow —this for the first time in years—without catching cold. After five months of treatment with increasing subcutaneous injections of egg-white and lactalbumin the skin reactions to lactalbumin gradually disappeared, but the egg-white still gave slightly positive reactions. At this time weak dilutions of egg, starting with 1 teaspoonful of egg-white to 1 quart of water, and milk, starting with a few drops, were given by mouth. After these were shown to be well tolerated they were gradually increased until after several months the boy took a whole egg and normal portions of milk. When the child began to get good portions of egg again he complained that the reason he did not like them was that they gave him a burning sensation in his mouth. At this time a second *x*-ray of the lungs was taken and marked diminution in infiltration was reported. Within the next six months of observation some interesting conditions arose. As he increased the quantity of egg and milk taken the boy developed several attacks, and after every attack the offending food was discontinued and injections were resumed, with prompt results. One attack came on after going in swimming while the boy was in the country. The mother, in her overzealousness to make up for lost time and to fatten

the boy, was giving him large amounts of fresh milk, about 2 quarts a day. His lactalbumin skin reaction, which had been negative for months, came back, showing a return of sensitivity. This, however, was soon overcome again by the aforementioned treatment. Another occurrence was the development of a severe attack of urticaria traced to the indulgence in three charlotte russes a day; it is surprising that no asthma developed at this time. The injections were continued until he was receiving dilutions of 1 : 100.

For the ensuing year the boy came to the clinic occasionally and reported excellent progress, with no attacks. His most recent visit after a period of two years showed his egg skin test still slightly positive and the lactalbumin negative. The boy retains his strong aversion for milk and eggs and eats them only moderately and in the preparation of other foods.

Summary.—A boy aged eleven years, a sufferer from asthma from babyhood, who originally had eczema when an infant. He reacted to egg-white and lactalbumin by skin tests. Rigid elimination of these articles of diet from his food, with subcutaneous injections of egg-white and lactalbumin, eventually effected a cure after a period of about one year in the sense that the patient partakes of these proteins freely as they are used in the preparation of his foods, and does not suffer from asthma after so doing unless he partakes of them to excess. The patient has been observed for one year subsequent to the year of treatment and partakes of a normal amount of egg and milk without ill effects.

Discussion.—It is possible that the original dose of egg-nog at two days of age may have passed through the permeable intestinal tract of the infant and laid the grounds for his future sensitizations. This, of course, is a purely hypothetic consideration.

The history is not as definite as to exact detail as the former case because of the age of the child. But the relationship between eczema, urticaria, and asthma is again brought out.

Here again the importance is brought out of eliminating every possible form of food that the offending protein may be

present in. Park,[3] in an interesting case of milk sensitivity, also reports a child who got a severe reaction from the milk in the bread.

It is evident that after the period of observation that this patient has been subjected to he has been definitely shown to be able to tolerate a normal amount of egg and milk, but that excessiveness apparently does bring back a certain degree of his sensitiveness; this, however, is easily controlled.

That the results have entirely been due to desensitization by injection or that by the complete elimination of the offending proteins the patient has learned to tolerate these proteins we are not prepared to state. At the present moment too little is known of this most intricate phase of protein sensitization, namely, treatment by desensitization, and all that can be said in this instance is that this patient responded in a biologic sense to the treatment instituted.

GROUP II. ASTHMA DUE TO CHICKEN FEATHERS AND SHOWING THE IMPORTANCE OF DUST IN DIAGNOSIS

Case III.—T. P., a boy of ten years, who continually suffered from catarrhal symptoms and frequent colds since infancy, for the past six years has had attacks of asthma. The family history is negative, except for the father's sister, who suffers from hay-fever.

The family was in the habit of spending their summer vacations at the grandmother's farm, and during these periods—that is, from May until September—suffered his severest attacks. His attacks were always preceded by sneezing and running nose and usually lasted two to three days. In the periods between his attacks the boy usually had some nasal catarrhal symptoms. His attacks in the winter were extremely infrequent; however, since the past two years these winter attacks have become somewhat more frequent. At first it appeared to be a case of hay-fever, but the attacks, starting as early as May and continuing into the winter, made this probability rather indefinite.

Skin tests for the pollens were negative. The child was

tested with feathers, animal hairs, and common foods, and only a suggestive reaction was obtained for chicken feathers. The patient was retested for all these proteins, with similar results. On account of the suggestive reaction given to chicken feathers and of the strong tendency for his attacks on the farm, this particular protein was thought to be the most probable cause of his trouble. The patient was advised to continue his regular mode of life, and we requested that we be called when the child had his next attack, so that we might be better able to analyze the conditions that obtained during this period.

Two months elapsed and we were summoned to the child at the height of an attack which had begun twenty-four hours previously. After considerable questioning as to all that the patient had eaten and everything that he had done it was learned that the day before he had visited a cousin's home and there had a pillow fight. This seemed a clue, and further questioning proved that the child had had to stop fighting because of sneezing and markedly running nose. The child developed a cough and that night had an attack of asthma which was still present when we were called in. An injection of 10 minims of adrenalin gave the boy some relief.

We advised an immediate change from the chicken-feather pillows to silk floss, and the mother was asked to return to the office the following week with samples of the feathers from the boy's own pillow, that of his cousin, and the dust of the bedroom. The material from the pillows and dust gave a moderate positive reaction, and it was then decided to test samples from the grandmother's pillows, house dust, and chicken coop dust. These too gave a moderately positive reaction, the wheal being 4 mm.; however, there was a marked persistent erythema 3 cm. in diameter. A clinical test was then done in order to prove the case definitely because of the rather indefinite character of the skin reactions. The boy, much against his will, was asked to have another pillow fight. Again he sneezed and developed a running nose. He was then advised to sleep on his cousin's pillow, and for a period of thirteen days practically every night after he had been in bed for several hours he would

sneeze and complain of nasal discharge and a choked-up feeling. On the thirteenth night after his return to the feather pillows he had a definite attack of asthma.

All the feather pillows, stuffed comforters, etc., were removed from the home and replaced by floss pillows and blankets. Since this has been done the boy has been free from all symptoms of coryza and asthma.

During the summer months the boy had, of recent years, developed a moderate eczema of the hands, feet, and knees which cleared up entirely when he returned from the country. This point was explained by the fact that the patient was in the habit of cleaning out the chicken coop regularly for his grandmother.

Case IV.—R. L., boy aged six years, has had attacks of asthma for the past two years. His illness first began on a farm after he had had pertussis the preceding spring. This child's attacks were also more severe during the summer, but persisted into the winter as well.

The tests with the prepared proteins were also indefinite until extracts of the home dust and the child's chicken feather pillow were made, and in this instance a definite large positive reaction was obtained to both substances. Removal of all the pillows and a thorough renovation of the entire home gave prompt relief of all symptoms. In order to prove the specificity of the dust after the boy had been sleeping on floss pillows for one month and his bedroom dust was again extracted in 0.4 per cent. sodium hydroxid the skin reaction to this dust was negative, whereas a control test with the former dust was strongly positive.

Discussion of Cases III and IV.—The careful history taking is invaluable in this type of case in eliciting some suggestive substance that may be the cause, particularly where the regular protein skin tests are not definitely positive. The clue in these cases was given by the fact that they both suffered most markedly on the farm. In Case III a history of chronic coryza since infancy was obtained, which is suggestive of some dust-producing

substance such as feathers or rabbit hair as the etiologic factor, as I have emphasized in a previous communication.[4]

The pertussis preceding the asthma in Case IV suggests a possible lowering of the resistance of the respiratory organs. Histories of pneumonia and pertussis, although commonly obtained as antedating asthma, may be purely coincidental, and these conditions may, in truth, have been asthma wrongly diagnosed.

Dust has been shown recently by Vander Veer to play a dominant rôle in many cases of asthma. We have reported the case of a child whose asthma was due to the rabbit hair in the felt hat factory dust which adhered to the father's clothing and person. It is evident, therefore, that in our cases it was the presence of the specific protein of the rabbit hair and chicken feather particles respectively in the dusts which gave the positive reactions. This has been nicely brought out by the simple test in Case IV, who gave no reaction to the dust in his bedroom after the feather pillows had been removed. When a positive reaction is obtained to dust there is something in the environment of the dust that should be sought for and eliminated.

The eczema which developed on the hands and feet of Case III was in all probability due to the boy's activities in the chicken coop. Markley[5] reported a case of eczema due to contact with a guinea-pig, showing that contact with animal epidermals may produce skin reactions in a hypersensitive individual.

Treatment in these cases is gratifying, as elimination of the feathers is all that is necessary.

GROUP III. ECZEMA IN BREAST-FED INFANTS SHOWN TO BE DUE TO THE LACTALBUMIN OF COW'S MILK SUCCESSFULLY TREATED BY PARENTERAL INJECTIONS

Case V.—P. L. This infant was first seen at six weeks of age, with a marked excoriation of the diaper region, intertrigo, eczema of the face, back of the neck, and seborrheic eczema of the scalp. The infant has had this condition for the past four

weeks. The child is entirely breast fed, weighs 9 pounds, 12 ounces, and except for the eczema is in good health.

Positive skin tests were obtained to cow's milk and lactalbumin. The mother, who had been drinking milk to excess, was advised to discontinue milk *per se* from her diet, and in the succeeding two weeks the eczema improved markedly, even though the only medication used was albolene for cleansing purposes. Within the following week—that is, three weeks after the elimination of milk from the mother's diet—the eczema disappeared entirely. At two months of age subcutaneous injections of lactalbumin were commenced. The initial dose was 0.05 c.c. of a 1 : 10,000 dilution. These injections were given three times a week in increasing doses until two months later, when the child gave a negative reaction to milk and a slightly positive reaction to lactalbumin, the last dose having been 0.8 c.c. of a 1 : 1000 dilution. At this time one of the breast feedings was supplemented by a rational formula which was boiled for ten minutes. This formula was continued for three weeks. The injections were continued, and when the child was five months old he received his last injection—0.5 c.c. of a 1 : 500 dilution. The skin reaction to lactalbumin at this time was also negative. The mother gradually increased the number of formulæ; the time of boiling was gradually decreased until the child was taking a raw milk formula. There was absolutely no return of the eczema. The child was seen from time to time, and at ten months was taking milk without any recurrence of the eczema, and the skin tests were still negative.

Case VI.—S. L. An infant ten and a half months old who had a most marked, bleeding, crusted eczema over his entire face, scalp, arms, and back of neck, and moderate on legs. The patient had developed this condition in the past three months. The mother had occasional urticaria while she was pregnant and while she was nursing the child. The family history is otherwise negative. Up to seven months of age the child was entirely breast fed and had absolutely no eczema. During the period of breast feeding the mother gave a history of having

indulged excessively in milk and beef. At the age of seven months the child was given a supplementary bottle once and then twice a day, and from then on became markedly constipated and started the development of his eczema. The mother continued to complement her breast feedings with cow's milk and other foods, and the child's condition became progressively worse. At the time of the first visit he gave a positive reaction to cow's milk, lactalbumin, and a negative reaction to beef. The mother was advised to discontinue all milk from her diet and to do the same with the child, and at the sacrifice of his weight to keep him on the breast entirely. The eczema was of such a severe type that it was advisable to pin the child in bed and a 5 per cent. euresol in Lassar's paste was ordered for his lesions. The child was seen again in two days and showed a most marked clearing of the eczema.

This treatment was continued and in the following week there was still a slight persistence of the eczema, which we attributed to the bread and butter which the child was still getting; these also were discontinued and the child kept on the breast feedings only. A month after he had first been seen the eczema was entirely cleared. The child had to be weaned shortly after this, as the mother was in the second month of pregnancy. As we could not resume fresh cow's milk, a formula composed of condensed milk was prescribed and cereals and vegetables were gradually added to the diet.

Subcutaneous injections of lactalbumin were given as in the former case, in this case starting with 0.05 c.c. of a 1 : 100,000, as judged by the fact that there was a positive reaction given to a dilution of 1 : 10,000. The injections were given twice a week, and after a period of three months the last injection was 0.8 c.c. of a 1 : 1000 dilution. The tests had become absolutely negative for both milk and lactalbumin. The child was then given a boiled formula of fresh cow's milk, which was gradually given unboiled and undiluted. He was discharged at fifteen months able to take milk without the recurrence of eczema. At seventeen months he was retested, and the skin reactions were again negative; he was at this time taking a

normal amount of fresh cow's milk and was free of any eczema.

Discussion of Cases V and VI.—The problem of eczema in the breast-fed infant has always aroused considerable interest. As has been stated in the discussion of Case I, O'Keefe and Shannon have shown the possibility that infants may be sensitized to foreign proteins by the passage of these proteins through the mother's milk. Some experimental work has been done by Shannon to prove this with fairly convincing results. We have conducted similar experiments with questionable results. That the passage of foreign proteins through the breast milk is highly probable is shown by our 2 cases and many others that we could cite (but which will be left for a future communication). A recent report by Hermann[6] has shown that pollens may pass through cow's milk and that individuals who are sensitive to that pollen will give a positive reaction to this milk.

When one is confronted with a case of eczema in a breast-fed child and learns that the mother is indulging excessively in any particular food it is advisable to eliminate that particular food from her diet, and when a positive protein skin reaction is obtained it is absolutely essential to do this.

As has been discussed in Case II, the problem of desensitization by subcutaneous injections must await further study. However, these 2 cases are offered from a group of 7 which have been successfully desensitized by this method.

Schloss[7] successfully desensitized cases by giving minute, gradually increasing doses of the offending protein by mouth, with excellent results, and also by subcutaneous injections. Whether the latter method will be shown to be the more exact one and the one of preference is yet to be proved.

There is one phase of the treatment that has been used in conjunction with the desensitization that has not yet been discussed, namely, that of the use of cooked proteins. It is well known that a case sensitive to egg, for example, will get no reaction if the egg has been cooked for a half-hour; and a case sensitive to milk will in many instances be able to tolerate

boiled milk. The heating process in some way so changes the protein as to destroy its anaphylactogenic properties when used in animal anaphylactic experiments, and this may be the explanation for the fact that these cooked proteins are tolerated by sensitive individuals. It would be unwise, therefore, to give Dryco, for example, which is heated for only a few seconds, and expect a sensitive individual to be able to tolerate it. Whereas, condensed milk, Nestle's Food, or malted milk, which undergo prolonged heating at a high temperature, would be well tolerated. For this reason the choice of condensed milk and boiled milks was made in the above cases before the patients were entirely desensitized.

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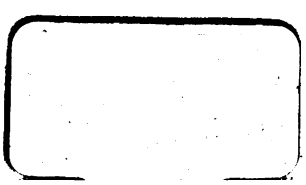

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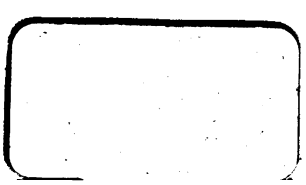

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